FIGURE 1

AGGCGGGCAGCAGCTGCAGGCTGACCTTGCAGCTTGGCGGA**ATG**GACTGGCCTCACAACCTGCTGTTTCTT
CTTACCATTTCCATCTTCCTGGGGCTGGGCCAGCCCAGGAGCCCCAAAAGCAAGAGGAAGGGGCAAGGGCG
GCCTGGGCCCCTGGCCCCTGGCCCTCACCAGGTGCCACTGGACCTGGTGTCACGGATGAAACCGTATGCCC
GCATGGAGGAGTATGAGAGGAACATCGAGGAGATGGTGGCCCAGCTGAGGAACAGCTCAGAGCTGGCCCAG
AGAAAGTGTGAGGTCAACTTGCAGCTGTGGATGTCCAACAAGAGGAGCCTGTCTCCCTGGGGCTACAGCAT
CAACCACGACCCCAGCCGTATCCCCGTGGACCTGCCGGAGGCACGGTGCCTGTGTCTGGGCTGTGTGAACC
CCTTCACCATGCAGGAGGACCGCAGCATGGTGAGCGTGCCGGTGTTCAGCCAGGTTCCTGTGCGCCGCCGC
CTCTGCCCGCCACCGCCCCGCACAGGGCCTTGCCGCCAGCGCGCAGTCATGGAGACCATCGCTGTGGGCTG
CACCTGCATCTTC**TGA**ATCACCTGGCCCAGAAGCCAGGCCAGCAGCCCGAGACCATCCTCCTTGCACCTTT
GTGCCAAGAAAGGCCTATGAAAAGTAAACACTGACTTTTGAAAGCAAG

FIGURE 2

MDWPHNLLFLLTISIFLGLGQPRSPKSKRKGQGRPGPLAPGPHQVPLDLVSRMKPYARMEEYERNIEEMVA
QLRNSSELAQRKCEVNLQLWMSNKRSLSPWGYSINHDPSRIPVDLPEARCLCLGCVNPFTMQEDRSMVSVP
VFSQVPVRRRLCPPPPRTGPCRQRAVMETIAVGCTCIF

FIGURE 3

GCCAGGTGTGCAGGCCGCTCCAAGCCCAGCCTGCCCCGCTGCCGCCACC**ATG**ACGCTCCTCCCCGGCCTCC
TGTTTCTGACCTGGCTGCACACATGCCTGGCCCACCATGACCCCTCCCTCAGGGGGCACCCCCACAGTCAC
GGTACCCCACACTGCTACTCGGCTGAGGAACTGCCCCTCGGCCAGGCCCCCCCACACCTGCTGGCTCGAGG
TGCCAAGTGGGGGCAGGCTTTGCCTGTAGCCCTGGTGTCCAGCCTGGAGGCAGCAAGCCACAGGGGGAGGC
ACGAGAGGCCCTCAGCTACGACCCAGTGCCCGGTGCTGCGGCCGGAGGAGGTGTTGGAGGCAGACACCCAC
CAGCGCTCCATCTCACCCTGGAGATACCGTGTGGACACGGATGAGGACCGCTATCCACAGAAGCTGGCCTT
CGCCGAGTGCCTGTGCAGAGGCTGTATCGATGCACGGACGGGCCGCGAGACAGCTGCGCTCAACTCCGTGC
GGCTGCTCCAGAGCCTGCTGGTGCTGCGCCGCCGGCCCTGCTCCCGCGACGGCTCGGGGCTCCCCACACCT
GGGGCCTTTGCCTTCCACACCGAGTTCATCCACGTCCCCGTCGGCTGCACCTGCGTGCTGCCCCGTTCAGT
G**TGA**CCGCCGAGGCCGTGGGGCCCCTAGACTGGACACGTGTGCTCCCCAGAGGGCACCCCCTATTTATGTG
TATTTATTGTTATTTATATGCCTCCCCCAACACTACCCTTGGGGTCTGGGCATTCCCCGTGTCTGGAGGAC
AGCCCCCCACTGTTCTCCTCATCTCCAGCCTCAGTAGTTGGGGGTAGAAGGAGCTCAGCACCTCTTCCAGC
CCTTAAAGCTGCAGAAAAGGTGTCACACGGCTGCCTGTACCTTGGCTCCCTGTCCTGCTCCCGGCTTCCCT
TACCCTATCACTGGCCTCAGGCCCCGCAGGCTGCCTCTTCCCAACCTCCTTGGAAGTACCCCTGTTTCTTA
AACAATTATTTAAGTGTACGTGTATTATTAAACTGATGAACACATCCCCAAAA

FIGURE 4

MTLLPGLLFLTWLHTCLAHHDPSLRGHPHSHGTPHCYSAEELPLGQAPPHLLARGAKWGQALPVALVSSLE
AASHRGRHERPSATTQCPVLRPEEVLEADTHQRSISPWRYRVDTDEDRYPQKLAFAECLCRGCIDARTGRE
TAALNSVRLLQSLLVLRRRPCSRDGSGLPTPGAFAFHTEFIHVPVGCTCVLPRSV

Signal peptide:	Amino acids 1-18
Tyrosine kinase phosphorylation site:	Amino acids 112-121
N-myristoylation sites:	Amino acids 32-38;55-61;133-139
Leucine zipper pattern:	Amino acids 3-25
Homologous region to IL-17:	Amino acids 99-195

FIGURE 5

GGCTTGCTGAAAATAAAATCAGGACTCCTAACCTGCTCCAGTCAGCCTGCTTCCACGAGGCCTGTCAGTCA
GTGCCCGACTTGTGACTGAGTGTGCAGTGCCCAGCATGTACCAGGTCAGTGCAGAGGGCTGCCTGAGGGCT
GTGCTGAGAGGGAGAGGAGCAGAGATGCTGCTGAGGGTGGAGGGAGGCCAAGCTGCCAGGTTTGGGGCTGG
GGGCCAAGTGGAGTGAGAAACTGGGATCCCAGGGGGAGGGTGCAG**ATG**AGGGAGCGACCCAGATTAGGTGA
GGACAGTTCTCTCATTAGCCTTTTCCTACAGGTGGTTGCATTCTTGGCAATGGTCATGGGAACCCACACCT
ACAGCCACTGGCCCAGCTGCTGCCCCAGCAAAGGGCAGGACACCTCTGAGGAGCTGCTGAGGTGGAGCACT
GTGCCTGTGCCTCCCCTAGAGCCTGCTAGGCCCAACCGCCACCCAGAGTCCTGTAGGGCCAGTGAAGATGGA
CCCCTCAACAGCAGGGCCATCTCCCCCTGGAGATATGAGTTGGACAGAGACTTGAACCGGCTCCCCCAGGA
CCTGTACCACGCCCGTTGCCTGTGCCCGCACTGCGTCAGCCTACAGACAGGCTCCCACATGGACCCCCGGG
GCAACTCGGAGCTGCTCTACCACAACCAGACTGTCTTCTACAGGCGGCCATGCCATGGCGAGAAGGGCACC
CACAAGGGCTACTGCCTGGAGCGCAGGCTGTACCGTGTTTCCTTAGCTTGTGTGTGTGTGCGGCCCCGTGT
GATGGGCTAGCCGGACCTGCTGGAGGCTGGTCCCTTTTTGGGAAACCTGGAGCCAGGTGTACAACCACTTG
CCATGAAGGGCCAGGATGCCCAGATGCTTGGCCCCTGTGAAGTGCTGTCTGGAGCAGCAGGATCCCGGGAC
AGGATGGGGGGCTTTGGGGAAAACCTGCACTTCTGCACATTTTGAAAAGAGCAGCTGCTGCTTAGGGCCGC
CGGAAGCTGGTGTCCTGTCATTTTCTCTCAGGAAAGGTTTTCAAAGTTCTGCCCATTTCTGGAGGCCACCA
CTCCTGTCTCTTCCTCTTTTCCCATCCCCTGCTACCCTGGCCCAGCACAGGCACTTTCTAGATATTTCCCC
CTTGCTGGAGAAGAAAGAGCCCCTGGTTTTATTTGTTTGTTTACTCATCACTCAGTGAGCATCTACTTTGG
GTGCATTCTAGTGTAGTTACTAGTCTTTTGACATGGATGATTCTGAGGAGGAAGCTGTTATTGAATGTATA
GAGATTTATCCAAATAAATATCTTTATTTAAAAATGAAAAA

FIGURE 6

MRERPRLGEDSSLISLFLQVVAFLAMVMGTHTYSHWPSCCPSKGQDTSEELLRWSTVPVPPLEPARPNRHP
ESCRASEDGPLNSRAISPWRYELDRDLNRLPQDLYHARCLCPHCVSLQTGSHMDPRGNSELLYHNQTVFYR
RPCHGEKGTHKGYCLERRLYRVSLACVCVRPRVMG

Signal peptide: Amino acids 1-32

N-glycosylation site: Amino acids 136-140

Tyrosine kinase phosphorylation site: Amino acids 127-135

N-myristoylation sites: Amino acids 44-50;150-156

FIGURE 7

ATGCTGGTAGCCGGCTTCCTGCTGGCGCTGCCGCCGAGCTGGGCCGCGGGCGCCCCCAGGGCGGGCAGGCG
CCCCGCGCGGCCGCGGGGCTGCGCGGACCGGCCGGAGGAGCTACTGGAGCAGCTGTACGGGCGCCTGGCGG
CCGGCGTGCTCAGTGCCTTCCACCACACGCTGCAGCTGGGGCCGCGTGAGCAGGCGCGCAACGCGAGCTGC
CCGGCAGGGGGCAGGCCCGGCGACCGCCGCTTCCGGCCGCCCACCAACCTGCGCAGCGTGTCGCCCTGGGC
CTACAGAATCTCCTACGACCCGGCGAGGTACCCCAGGTACCTGCCTGAAGCCTACTGCCTGTGCCGGGGCT
GCCTGACCGGGCTGTTCGGCGAGGAGGACGTGCGCTTCCGCAGCGCCCCTGTCTACATGCCCACCGTCGTC
CTGCGCCGCACCCCCGCCTGCGCCGGCGGCCGTTCCGTCTACACCGAGGCCTACGTCACCATCCCCGTGGG
CTGCACCTGCGTCCCCGAGCCGGAGAAGGACGCAGACAGCATCAACTCCAGCATCGACAAACAGGGCGCCA
AGCTCCTGCTGGGCCCCAACGACGCGCCCGCTGGCCCCTGAGGCCGGTCCTGCCCCGGGAGGTCTCCCCGG
CCCGCATCCCGAGGCGCCCAAGCTGGAGCCGCCTGGAGGGCTCGGTCGGCGACCTCTGAAGAGAGTGCACC
GAGCAAACCAAGTGCCGGAGCACCAGCGCCGCCTTTCCATGGAGACTCGTAAGCAGCTTCATCTGACACGG
GCATCCCTGGCTTGCTTTTAGCTACAAGCAAGCAGCGTGGCTGGAAGCTGATGGGAAACGACCCGGCACGG
GCATCCTGTGTGCGGCCCGCATGGAGGGTTTGGAAAAGTTCACGGAGGCTCCCTGAGGAGCCTCTCAGATC
GGCTGCTGCGGGTGCAGGGCGTGACTCACCGCTGGGTGCTTGCCAAAGAGATAGGGACGCATATGCTTTTT
AAAGCAATCTAAAAATAATAATAAGTATAGCGACTATATACCTACTTTTAAAATCAACTGTTTTGAATAGA
GGCAGAGCTATTTTATATTATCAAATGAGAGCTACTCTGTTACATTTCTTAACATATAAACATCGTTTTTT
ACTTCTTCTGGTAGAATTTTTTAAAGCATAATTGGAATCCTTGGATAAATTTTGTAGCTGGTACACTCTGG
CCTGGGTCTCTGAATTCAGCCTGTCACCGATGGCTGACTGATGAAATGGACACGTCTCATCTGACCCACTC
TTCCTTCCACTGAAGGTCTTCACGGGCCTCCAGGTGGACCAAAGGGATGCACAGGCGGCTCGCATGCCCCA
GGGCCAGCTAAGAGTTCCAAAGATCTCAGATTTGGTTTTAGTCATGAATACATAAACAGTCTCAAACTCGC
ACAATTTTTTCCCCCTTTTGAAAGCCACTGGGGCCAATTTGTGGTTAAGAGGTGGTGAGATAAGAAGTGGA
ACGTGACATCTTTGCCAGTTGTCAGAAGAATCCAAGCAGGTATTGGCTTAGTTGTAAGGGCTTTAGGATCA
GGCTGAATATGAGGACAAAGTGGGCCACGTTAGCATCTGCAGAGATCAATCTGGAGGCTTCTGTTTCTGCA
TTCTGCCACGAGAGCTAGGTCCTTGATCTTTTCTTTAGATTGAAAGTCTGTCTCTGAACACAATTATTTGT
AAAAGTTAGTAGTTCTTTTTTAAATCATTAAAAGAGGCTTGCTGAAGGAT

FIGURE 8

MLVAGFLLALPPSWAAGAPRAGRRPARPRGCADRPEELLEQLYGRLAAGVLSAFHHTLQLGPREQARNASC
PAGGRPGDRRFRPPTNLRSVSPWAYRISYDPARYPRYLPEAYCLCRGCLTGLFGEEDVRFRSAPVYMPTVV
LRRTPACAGGRSVYTEAYVTIPVGCTCVPEPEKDADSINSSIDKQGAKLLLGPNDAPAGP

Signal peptide:	Amino acids 1-15
N-glycosylation sites:	Amino acids 68-72;181-185
Tyrosine kinase phosphorylation site:	Amino acids 97-106
N-myristoylation sites:	Amino acids 17-23;49-55;74-80; 118-124
Amidation site:	Amino acids 21-25

FIGURE 9

CAACTGCACCTCGGTTCTATCGATAGCCACCAGCGCAAC**ATG**ACAGTGAAGACCCTGCATGGCCCAGCCAT
GGTCAAGTACTTGCTGCTGTCGATATTGGGGCTTGCCTTTCTGAGTGAGGCGGCAGCTCGGAAAATCCCCA
AAGTAGGACATACTTTTTTCCAAAAGCCTGAGAGTTGCCCGCCTGTGCCAGGAGGTAGTATGAAGCTTGAC
ATTGGCATCATCAATGAAAACCAGCGCGTTTCCATGTCACGTAACATCGAGAGCCGCTCCACCTCCCCCTG
GAATTACACTGTCACTTGGGACCCCAACCGGTACCCCTCGGAAGTTGTACAGGCCCAGTGTAGGAACTTGG
GCTGCATCAATGCTCAAGGAAAGGAAGACATCTCCATGAATTCCGTTCCCATCCAGCAAGAGACCCTGGTCGTC
CGGAGGAAGCACCAAGGCTGCTCTGTTTCTTTCCAGTTGGAGAAGGTGCTGGTGACTGTTGGCTGCACCTG
CGTCACCCCTGTCATCCACCATGTGCAGTAAGAGGTGCATATCCACTCAGCTGAAGAAG

FIGURE 10

MTVKTLHGPAMVKYLLLSILGLAFLSEAAARKIPKVGHTFFQKPESCPPVPGGSMKLDIGIINENQRVSMS
RNIESRSTSPWNYTVTWDPNRYPSEVVQAQCRNLGCINAQGKEDISMNSVPIQQETLVVRRKHQGCSVSFQ
LEKVLVTVGCTCVTPVIHHVQ

Signal sequence:	Amino acids 1-30
N-glycosylation site:	Amino acids 83-86
N-myristoylation sites:	Amino acids 106-111;136-141

FIGURE 11

CCGGCG**ATG**TCGCTCGTGCTGCTAAGCCTGGCCGCGCTGTGCAGGAGCGCCGTACCCCGAGAGCCGACCGT
TCAATGTGGCTCTGAAACTGGGCCATCTCCAGAGTGGATGCTACAACATGATCTAATCCCCGGAGACTTGA
GGGACCTCCGAGTAGAACCTGTTACAACTAGTGTTGCAACAGGGGACTATTCAATTTTGATGAATGTAAGC
TGGGTACTCCGGGCAGATGCCAGCATCCGCTTGTTGAAGGCCACCAAGATTTGTGTGACGGGCAAAAGCAA
CTTCCAGTCCTACAGCTGTGTGAGGTGCAATTACACAGAGGCCTTCCAGACTCAGACCAGACCCTCTGGTG
GTAAATGGACATTTTCCTACATCGGCTTCCCTGTAGAGCTGAACACAGTCTATTTCATTGGGGCCCATAAT
ATTCCTAATGCAAATATGAATGAAGATGGCCCTTCCATGTCTGTGAATTTCACCTCACCAGGCTGCCTAGA
CCACATAATGAAATATAAAAAAAAGTGTGTCAAGGCCGGAAGCCTGTGGGATCCGAACATCACTGCTTGTA
AGAAGAATGAGGAGACAGTAGAAGTGAACTTCACAACCACTCCCCTGGGAAACAGATACATGGCTCTTATC
CAACACAGCACTATCATCGGGTTTTCTCAGGTGTTTGAGCCACACCAGAAGAAACAAACGCGAGCTTCAGT
GGTGATTCCAGTGACTGGGGATAGTGAAGGTGCTACGGTGCAGCTGACTCCATATTTTCCTACTTGTGGCA
GCGACTGCATCCGACATAAAGGAACAGTTGTGCTCTGCCCACAAACAGGCGTCCCTTTCCCTCTGGATAAC
AACAAAAGCAAGCCGGGAGGCTGGCTGCCTCTCCTCCTGCTGTCTCTGCTGGTGGCCACATGGGTGCTGGT
GGCAGGGATCTATCTAATGTGGAGGCACGAAAGGATCAAGAAGACTTCCTTTTCTACCACCACACTACTGC
CCCCCATTAAGGTTCTTGTGGTTTACCCATCTGAAATATGTTTCCATCACACAATTTGTTACTTCACTGAA
TTTCTTCAAAACCATTGCAGAAGTGAGGTCATCCTTGAAAAGTGGCAGAAAAAGAAAATAGCAGAGATGGG
TCCAGTGCAGTGGCTTGCCACTCAAAAGAAGGCAGCAGACAAAGTCGTCTTCCTTCTTTCCAATGACGTCA
ACAGTGTGTGCGATGGTACCTGTGGCAAGAGCGAGGGCAGTCCCAGTGAGAACTCTCAAGACCTCTTCCCC
CTTGCCTTTAACCTTTTCTGCAGTGATCTAAGAAGCCAGATTCATCTGCACAAATACGTGGTGGTCTACTT
TAGAGAGATTGATACAAAAGACGATTACAATGCTCTCAGTGTCTGCCCCAAGTACCACCTCATGAAGGATG
CCACTGCTTTCTGTGCAGAACTTCTCCATGTCAAGCAGCAGGTGTCAGCAGGAAAAAGATCACAAGCCTGC
CACGATGGCTGCTGCTCCTTGTAG

FIGURE 12

MSLVLLSLAALCRSAVPREPTVQCGSETGPSPEWMLQHDLIPGDLRDLRVEPVTTSVATGDYSILMNVSWV
LRADASIRLLKATKICVTGKSNFQSYSCVRCNYTEAFQTQTRPSGGKWTFSYIGFPVELNTVYFIGAHNIP
NANMNEDGPSMSVNFTSPGCLDHIMKYKKKCVKAGSLWDPNITACKKNEETVEVNFTTTPLGNRYMALIQH
STIIGFSQVFEPHQKKQTRASVVIPVTGDSEGATVQLTPYFPTCGSDCIRHKGTVVLCPQTGVPFPLDNNK
SKPGGWLPLLLLSLLVATWVLVAGIYLMWRHERIKKTSFSTTTLLPPIKVLVVYPSEICFHHTICYFTEFL
QNHCRSEVILEKWQKKKIAEMGPVQWLATQKKAADKVVFLLSNDVNSVCDGTCGKSEGSPSENSQDLFPLA
FNLFCSDLRSQIHLHKYVVVYFREIDTKDDYNALSVCPKYHLMKDATAFCAELLHVKQQVSAGKRSQACHD
GCCSL

Signal sequence:	Amino acids 1-14
Transmembrane domain:	Amino acids 290-309
N-glycosylation sites:	Amino acids 67-70;103-106;156-159; 183-186;197-200;283-286
cAMP- and cGMP-dependent protein kinase phosphorylation sites:	Amino acids 228-231;319-322
N-myristoylation site:	Amino acids 116-121
Amidation site:	Amino acids 488-491

FIGURE 13

ACACTGGCCAAACAAAAACGAAAGCACTCCGTGCTGGAAGTAGGAGGAGAGTCAGGACTCCCAGGACAGAG
AGTGCACAAACTACCCAGCACAGCCCCCTCCGCCCCCTCTGGAGGCTGAAGAGGGATTCCAGCCCCTGCCA
CCCACAGACACGGGCTGACTGGGGTGTCTGCCCCCCTTGGGGGGGGGCAGCACAGGGCCTCAGGCCTGGGT
GCCACCTGGCACCTAGAAG**ATG**CCTGTGCCCTGGTTCTTGCTGTCCTTGGCACTGGGCCGAAGCCCAGTGG
TCCTTTCTCTGGAGAGGCTTGTGGGGCCTCAGGACGCTACCCACTGCTCTCCGGGCCTCTCCTGCCGCCTC
TGGGACAGTGACATACTCTGCCTGCCTGGGGACATCGTGCCTGCTCCGGGCCCCGTGCTGGCGCCTACGCA
CCTGCAGACAGAGCTGGTGCTGAGGTGCCAGAAGGAGACCGACTGTGACCTCTGTCTGCGTGTGGCTGTCC
ACTTGGCCGTGCATGGGCACTGGGAAGAGCCTGAAGATGAGGAAAAGTTTGGAGGAGCAGCTGACTCAGGG
GTGGAGGAGCCTAGGAATGCCTCTCTCCAGGCCCAAGTCGTGCTCTCCTTCCAGGCCTACCCTACTGCCCG
CTGCGTCCTGCTGGAGGTGCAAGTGCCTGCTGCCCTTGTGCAGTTTGGTCAGTCTGTGGGCTCTGTGGTATAT
GACTGCTTCGAGGCTGCCCTAGGGAGTGAGGTACGAATCTGGTCCTATACTCAGCCCAGGTACGAGAAGGA
ACTCAACCACACACAGCAGCTGCCTGCCCTGCCCTGGCTCAACGTGTCAGCAGATGGTGACAACGTGCATC
TGGTTCTGAATGTCTCTGAGGAGCAGCACTTCGGCCTCTCCCTGTACTGGAATCAGGTCCAGGGCCCCCCA
AAACCCCGGTGGCACAAAAACCTGACTGGACCGCAGATCATTACCTTGAACCACACAGACCTGGTTCCCTG
CCTCTGTATTCAGGTGTGGCCTCTGGAACCTGACTCCGTTAGGACGAACATCTGCCCCTTCAGGGAGGACC
CCCGCGCACACCAGAACCTCTGGCAAGCCGCCCGACTGCGACTGCTGACCCTGCAGAGCTGGCTGCTGGAC
GCACCGTGCTCGCTGCCCGCAGAAGCGGCACTGTGCTGGCGGGCTCCGGGTGGGGACCCCTGCCAGCCACT
GGTCCCACCGCTTTCCTGGGAGAACGTCACTGTGGACAAGGTTCTCGAGTTCCCATTGCTGAAAGGCCACC
CTAACCTCTGTGTTCAGGTGAACAGCTCGGAGAAGCTGCAGCTGCAGGAGTGCTTGTGGGCTGACTCCCTG
GGGCCTCTCAAAGACGATGTGCTACTGTTGGAGACACGAGGCCCCCAGGACAACAGATCCCTCTGTGCCTT
GGAACCCAGTGGCTGTACTTCACTACCCAGCAAAGCCTCCACGAGGGCAGCTCGCCTTGGAGAGTACTTAC
TACAAGACCTGCAGTCAGGCCAGTGTCTGCAGCTATGGGACGATGACTTGGGAGCGCTATGGGCCTGCCCC
ATGGACAAATACATCCACAAGCGCTGGGCCCTCGTGTGGCTGGCCTGCCTACTCTTTGCCGCTGCGCTTTC
CCTCATCCTCCTTCTCAAAAAGGATCACGCGAAAGGGTGGCTGAGGCTCTTGAAACAGGACGTCCGCTCGG
GGGCGGCCGCCAGGGGCCGCGCGGCTCTGCTCCTCTACTCAGCCGATGACTCGGGTTTCGAGCGCCTGGTG
GGCGCCCTGGCGTCGGCCCTGTGCCAGCTGCCGCTGCGCGTGGCCGTAGACCTGTGGAGCCGTCGTGAACT
GAGCGCGCAGGGGCCCGTGGCTTGGTTTCACGCGCAGCGGCGCCAGACCCTGCAGGAGGGCGGCGTGGTGG
TCTTGCTCTTCTCTCCCGGTGCGGTGGCGCTGTGCAGCGAGTGGCTACAGGATGGGGTGTCCGGGCCCGGG
GCGCACGGCCCGCACGACGCCTTCCGCGCCTCGCTCAGCTGCGTGCTGCCCGACTTCTTGCAGGGCCGGGC
GCCCGGCAGCTACGTGGGGGCCTGCTTCGACAGGCTGCTCCACCCGGACGCCGTACCCGCCCTTTTCCGCA
CCGTGCCCGTCTTCACACTGCCCTCCCAACTGCCAGACTTCCTGGGGGCCCTGCAGCAGCCTCGCGCCCCG
CGTTCCGGGCGGCTCCAAGAGAGAGCGGAGCAAGTGTCCCGGGCCCTTCAGCCAGCCCTGGATAGCTACTT
CCATCCCCCGGGGACTCCCGCGCCGGGACGCGGGGTGGGACCAGGGGCGGGACCTGGGGCGGGGGACGGGA
CTTAAATAAAGGCAGACGCTGTTTTTCTAAAAAAA

FIGURE 14

MPVPWFLLSLALGRSPVVLSLERLVGPQDATHCSPGLSCRLWDSDILCLPGDIVPAPGPVLAPTHLQTELV
LRCQKETDCDLCLRVAVHLAVHGHWEEPEDEEKFGGAADSGVEEPRNASLQAQVVLSFQAYPTARCVLLEV
QVPAALVQFGQSVGSVVYDCFEAALGSEVRIWSYTQPRYEKELNHTQQLPALPWLNVSADGDNVHLVLNVS
EEQHFGLSLYWNQVQGPPKPRWHKNLTGPQIITLNHTDLVPCLCIQVWPLEPDSVRTNICPFREDPRAHQN
LWQAARLRLLTLQSWLLDAPCSLPAEAALCWRAPGGDPCQPLVPPLSWENVTVDKVLEFPLLKGHPNLCVQ
VNSSEKLQLQECLWADSLGPLKDDVLLLETRGPQDNRSLCALEPSGCTSLPSKASTRAARLGEYLLQDLQS
GQCLQLWDDDLGALWACPMDKYIHKRWALVWLACLLFAAALSLILLLKKDHAKGWLRLLKQDVRSGAAARG
RAALLLYSADDSGFERLVGALASALCQLPLRVAVDLWSRRELSAQGPVAWFHAQRRQTLQEGGVVVLLFSP
GAVALCSEWLQDGVSGPGAHGPHDAFRASLSCVLPDFLQGRAPGSYVGACFDRLLHPDAVPALFRTVPVFT
LPSQLPDFLGALQQPRAPRSGRLQERAEQVSRALQPALDSYFHPPGTPAPGRGVGPGAGPGAGDGT

signal sequence:	Amino acids 1-20
transmembrane domain:	Amino acids 453-473
N-glycosylation sites:	Amino acids 118-121;186-189;198-201; 211-214;238-241;248-251;334-337; 357-360;391-394
Glycosaminoglycan attachment site:	Amino acids 583-586
cAMP- and cGMP-dependent protein kinase phosphorylation site:	Amino acids 552-555
N-myristoylation sites:	Amino acids 107-112;152-157;319-324; 438-443;516-521;612-617;692-697; 696-701;700-705

FIGURE 15

CGAGGGCTCCTGCTGGTACTGTGTTCGCTGCTGCACAGCAAGGCCCTGCCACCCACCTTCAGGCCATGCAG
CCATGTTCCGGGAGCCCTAATTGCACAGAAGCCC**ATG**GGGAGCTCCAGACTGGCAGCCCTGCTCCTGCCTC
TCCTCCTCATAGTCATCGACCTCTCTGACTCTGCTGGGATTGGCTTTCGCCACCTGCCCCACTGGAACACC
CGCTGTCCTCTGGCCTCCCACACGGATGACAGTTTCACTGGAAGTTCTGCCTATATCCCTTGCCGCACCTG
GTGGGCCCTCTTCTCCACAAAGCCTTGGTGTGTGCGAGTCTGGCACTGTTCCCGCTGTTTGTGCCAGCATCTGC
TGTCAGGTGGCTCAGGTCTTCAACGGGGCCTCTTCCACCTCCTGGTGCAGAAATCCAAAAAGTCTTCCACA
TTCAAGTTCTATAGGAGACACAAGATGCCAGCACCTGCTCAGAGGAAGCTGCTGCCTCGTCGTCACCTGTC
TGAGAAGAGCCATCACATTTCCATCCCCTCCCCAGACATCTCCCACAAGGGACTTCGCTCTAAAAGGACCC
AACCTTCGGATCCAGAGACATGGGAAAGTCTTCCCAGATTGGACTCACAAAGGCATGGAGGACCCGAGTTC
TCCTTTGATTTGCTGCCTGAGGCCCGGGCTATTCGGGTGACCATATCTTCAGGCCCTGAGGTCAGCGTGCG
TCTTTGTCACCAGTGGGCACTGGAGTGTGAAGAGCTGAGCAGTCCCTATGATGTCCAGAAAATTGTGTCTG
GGGGCCACACTGTAGAGCTGCCTTATGAATTCCTTCTGCCCTGTCTGTGCATAGAGGCATCCTACCTGCAA
GAGGACACTGTGAGGCGCAAAAAATGTCCCTTCCAGAGCTGGCCAGAAGCCTATGGCTCGGACTTCTGGAA
GTCAGTGCACTTCACTGACTACAGCCAGCACACTCAGATGGTCATGGCCCTGACACTCCGCTGCCCACTGA
AGCTGGAAGCTGCCCTCTGCCAGAGGCACGACTGGCATACCCTTTGCAAAGACCTCCCGAATGCCACGGCT
CGAGAGTCAGATGGGTGGTATGTTTTGGAGAAGGTGGACCTGCACCCCCAGCTCTGCTTCAAGTTCTCTTT
TGGAAACAGCAGCCATGTTGAATGCCCCCACCAGACTGGGTCTCTCACATCCTGGAATGTAAGCATGGATA
CCCAAGCCCAGCAGCTGATTCTTCACTTCTCCTCAAGAATGCATGCCACCTTCAGTGCTGCCTGGAGCCTC
CCAGGCTTGGGGCAGGACACTTTGGTGCCCCCCGTGTACACTGTCAGCCAGGCCCGGGGCTCAAGCCCAGT
GTCACTAGACCTCATCATTCCCTTCCTGAGGCCAGGGTGCTGTGTCCTGGTGTGGCGGTCAGATGTCCAGT
TTGCCTGGAAGCACCTCTTGTGTCCAGATGTCTCTTACAGACACCTGGGGCTCTTGATCCTGGCACTGCTG
GCCCTCCTCACCCTACTGGGTGTTGTTCTGGCCCTCACCTGCCGGCGCCCACAGTCAGGCCCGGGCCCAGC
GCGGCCAGTGCTCCTCCTGCACGCGGCGGACTCGGAGGCGCAGCGGCGCCTGGTGGGAGCGCTGGCTGAAC
TGCTACGGGCAGCGCTGGGCGGCGGGCGCGACGTGATCGTGGACCTGTGGGAGGGGAGGCACGTGGCGCGCGT
GGGCCCGCTGCCGTGGCTCTGGGCGGCGCGGACGCGCGTAGCGCGGGAGCAGGGCACTGTGCTGCTGCTGT
GGAGCGGCGCCGACCTTCGCCCGGTCAGCGGCCCCGACCCCCGCGCCGCGCCCCTGCTCGCCCTGCTCCAC
GCTGCCCCGCGCCCGCTGCTGCTGCTCGCTTACTTCAGTCGCCTCTGCGCCAAGGGCGACATCCCCCCGCC
GCTGCGCGCCCTGCCGCGCTACCGCCTGCTGCGCGACCTGCCGCGTCTGCTGCGGGCGCTGGACGCGCGGC
CTTTCGCAGAGGCCACCAGCTGGGGCCGCCTTGGGGCGCGGCAGCGCAGGCAGAGCCGCCTAGAGCTGTGC
AGCCGGCTTGAACGAGAGGCCGCCCGACTTGCAGACCTAGGTTGAGCAGAGCTCCACCGCAGTCCCGGGTGTCT

FIGURE 16

MGSSRLAALLLPLLLIVIDLSDSAGIGFRHLPHWNTRCPLASHTDDSFTGSSAYIPCRTWWALFSTKPWCV
RVWHCSRCLCQHLLSGGSGLQRGLFHLLVQKSKKSSTFKFYRRHKMPAPAQRKLLPRRHLSEKSHHISIPS
PDISHKGLRSKRTQPSDPETWESLPRLDSQRHGGPEFSFDLLPEARAIRVTISSGPEVSVRLCHQWALECE
ELSSPYDVQKIVSGGHTVELPYEFLLPCLCIEASYLQEDTVRRKKCPFQSWPEAYGSDFWKSVHFTDYSQH
TQMVMALTLRCPLKLEAALCQRHDWHTLCKDLPNATARESDGWYVLEKVDLHPQLCFKFSFGNSSHVECPH
QTGSLTSWNVSMDTQAQQLILHFSSRMHATFSAAWSLPGLGQDTLVPPVYTVSQARGSSPVSLDLIIPFLR
PGCCVLVWRSDVQFAWKHLLCPDVSYRHLGLLILALLALLTLLGVVLALTCRRPQSGPGPARPVLLLHAAD
SEAQRRLVGALAELLRAALGGGRDVIVDLWEGRHVARVGPLPWLWAARTRVAREQGTVLLLWSGADLRPVS
GPDPRAAPLLALLHAAPRPLLLLAYFSRLCAKGDIPPPLRALPRYRLLRDLPRLLRALDARPFAEATSWGR
LGARQRRQSRLELCSRLEREAARLADLG

Signal peptide: Amino acids 1-23

Transmembrane domain: Amino acids 455-472

N-glycosylation sites: Amino acids 318-322;347-351;364-368

Glycosaminoglycan attachment site: Amino acids 482-486

cAMP- and cGMP-dependent protein kinase phosphorylation sites:
Amino acids 104-108;645-649

Tyrosine kinase phosphorylation site: Amino acids 322-329

N-myristoylation sites: Amino acids 90-96;358-364;470-476

Eukaryotic cobalamin-binding proteins: Amino acids 453-462

FIGURE 17

GCCAGGCCCTATCTCCCTGCCAGGAGGCCGGAGTGGGGGAGGTCAGACGGGGCGGTTGGAGGGGGAGGGATG
CCACGCGCTTCTGCCTCAGGTGTTCCTGCGTTGTTTGTCAGTGGAGAGCAGGGAGTGGGGCCAGCCAGCA
GAAACAGTGGGCTGTACAACATCACCTTCAAATATGACAATTGTACCACCTACTTGAATCCAGTGGGGAAG
CATGTGATTGCTGACGCCCAGAATATCACCATCAGCCAGTATGCTTGCCATGACCAAGTGGCAGTCACCAT
TCTTTGGTCCCCAGGGGCCCTCGGCATCGAATTCCTGAAAGGATTTCGGGTAATACTGGAGGAGCTGAAGT
CGGAGGGAAGACAGTGCCAACAACTGATTCTAAAGGATCCGAAGCAGCTCAACAGTAGCTTCAAAAGAACT
GGAATGGAATCTCAACCTTTCCTGAATATGAAATTTGAAACGGATTATTTCGTAAAGGTTGTCCCTTTTCC
TTCCATTAAAAACGAAAGCAATTACCACCCTTTCTTCTTTAGAACCCGAGCCTGTGACCTGTTGTTACAGC
CGGACAATCTAGCTTGTAAACCCTTCTGGAAGCCTCGGAACCTGAACATCAGCCAGCATGGCTCGGACATGC
AGGTGTCCTTCGACCACGCACCGCATGGCTCGGACATGCAGGTGTCCTTCGACCACGCACCGCACAACTTC
GGCTTCCGTTTCTTCTATCTTCACTACAAGCTCAAGCACGAAGGACCTTTCAAGCGAAAGACCTGTAAGCA
GGAGCAAACTACAGAGATGACCAGCTGCCTCCTTCAAAATGTTTCTCCAGGGGATTATATAATTGAGCTGG
TGGATGACACTAACACAACAAGAAAAGTGATGCATTATGCCTTAAAGCCAGTGCACTCCCCGTGGGCCGGG
CCCATCAGAGCCGTGGCCATCACAGTGCCACTGGTAGTCATATCGGCATTCGCGACGCTCTTCACTGTGAT
GTGCCGCAAGAAGCAACAAGAAAATATATATTCACATTTAGATGAAGAGAGCTCTGAGTCTTCCACATACA
CTGCAGCACTCCCAAGAGAGAGGCTCCGGCCGCGGCCGAAGGTCTTTCTCTGCTATTCCAGTAAAGATGGC
CAGAATCACATGAATGTCGTCCAGTGTTTCGCCTACTTCCTCCAGGACTTCTGTGGCTGTGAGGTGGCTCT
GGACCTGTGGGAAGACTTCAGCCTCTGTAGAGAAGGGCAGAGAGAATGGGTCATCCAGAAGATCCACGAGT
CCCAGTTCATCATTGTGGTTTGTTCCAAAGGTATGAAGTACTTTGTGGACAAGAAGAACTACAAACACAAA
GGAGGTGGCCGAGGCTCGGGGAAAGGAGAGCTCTTCCTGGTGGCGGTGTCAGCCATTGCCGAAAAGCTCCG
CCAGGCCAAGCAGAGTTCGTCCGCGGCGCTCAGCAAGTTTATCGCCGTCTACTTTGATTATTCCTGCGAGG
GAGACGTCCCCGGTATCCTAGACCTGAGTACCAAGTACAGACTCATGGACAATCTTCCTCAGCTCTGTTCC
CACCTGCACTCCCGAGACCACGGCCTCCAGGAGCCGGGGCAGCACACGCGACAGGGCAGCAGAAGGAACTA
CTTCCGGAGCAAGTCAGGCCGGTCCCTATACGTCGCCATTTGCAACATGCACCAGTTTATTGACGAGGAGC
CCGACTGGTTCGAAAAGCAGTTCGTTCCCTTCCATCCTCCTCCACTGCGCTACCGGGAGCCAGTCTTGGAG
AAATTTGATTCGGGCTTGGTTTTAAATGATGTCATGTGCAAACCAGGGCCTGAGAGTGACTTCTGCCTAAA
GGTAGAGGCGGCTGTTCTTGGGGCAACCGGACCAGCCGACTCCCAGCACGAGAGTCAGCATGGGGGCCTGG
ACCAAGACGGGGAGGCCCGGCCTGCCCTTGACGGTAGCGCCGCCCTGCAACCCCTGCTGCACACGGTGAAA
GCCGGCAGCCCCTCGGACATGCCGCGGGACTCAGGCATCTATGACTCGTCTGTGCCCTCATCCGAGCTGTC
TCTGCCACTGATGGAAGGACTCTCGACGGACCAGACAGAAACGTCTTCCCTGACGGAGAGCGTGTCCTCCT
CTTCAGGCCTGGGTGAGGAGGAACCTCCTGCCCTTCCTTCCAAGCTCCTCTCTTCTGGGTCATGCAAAGCA
GATCTTGGTTGCCGCAGCTACACTGATGAACTCCACGCGGTCGCCCCTTTGTAACAAAACGAAAGAGTCTA
AGCATTGCCACTTTAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA

FIGURE 18

MPRASASGVPALFVSGEQGVGPASRNSGLYNITFKYDNCTTYLNPVGKHVIADAQNITISQYACHDQVAVT
ILWSPGALGIEFLKGFRVILEELKSEGRQCQQLILKDPKQLNSSFKRTGMESQPFLNMKFETDYFVKVVPF
PSIKNESNYHPFFFRTRACDLLLQPDNLACKPFWKPRNLNISQHGSDMQVSFDHAPHGSDMQVSFDHAPHN
FGFRFFYLHYKLKHEGPFKRKTCKQEQTTEMTSCLLQNVSPGDYIIELVDDTNTTRKVMHYALKPVHSPWA
GPIRAVAITVPLVVISAFATLFTVMCRKKQQENIYSHLDEESSESSTYTAALPRERLRPRPKVFLCYSSKD
GQNHMNVVQCFAYFLQDFCGCEVALDLWEDFSLCREGQREWVIQKIHESQFIIVVCSKGMKYFVDKKNYKH
KGGGRGSGKGELFLVAVSAIAEKLRQAKQSSSAALSKFIAVYFDYSCEGDVPGILDLSTKYRLMDNLPQLC
SHLHSRDHGLQEPGQHTRQGSRRNYFRSKSGRSLYVAICNMHQFIDEEPDWFEKQFVPFHPPPLRYREPVL
EKFDSGLVLNDVMCKPGPESDFCLKVEAAVLGATGPADSQHESQHGGLDQDGEARPALDGSAALQPLLHTV
KAGSPSDMPRDSGIYDSSVPSSELSLPLMEGLSTDQTETSSLTESVSSSSGLGEEEPPALPSKLLSSGSCK
ADLGCRSYTDELHAVAPL

Transmembrane domain: Amino acids 283-307

N-glycosylation sites: Amino acids 31-34;38-41;56-59;
113-116;147-150;182-185;266-269

Glycosaminoglycan attachment sites: Amino acids 433-436;689-692

cAMP- and cGMP-dependent protein kinase phosphorylation:
Amino acids 232-235

Tyrosine kinase phosphorylation sites: Amino acids 312-319;416-424

N-myristoylation site: Amino acids 19-24;375-380;428-433;
429-434;432-437;517-522;574-579;
652-657;707-712

FIGURE 19

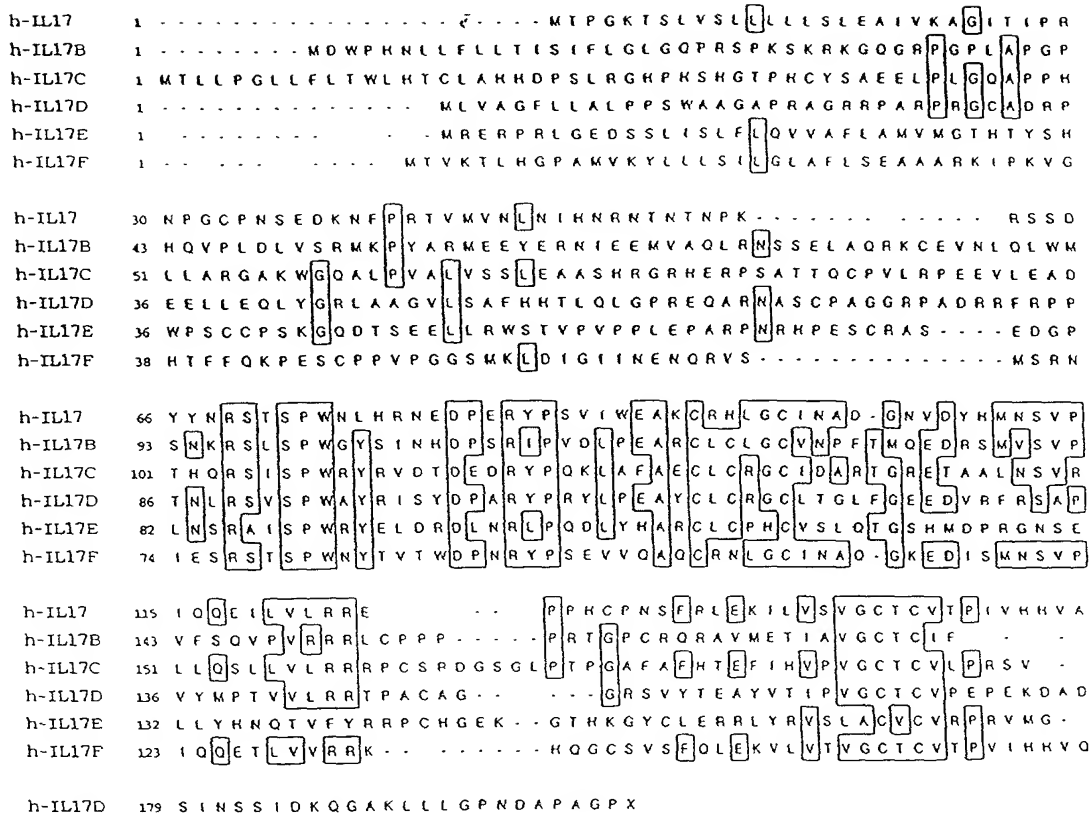


FIGURE 20

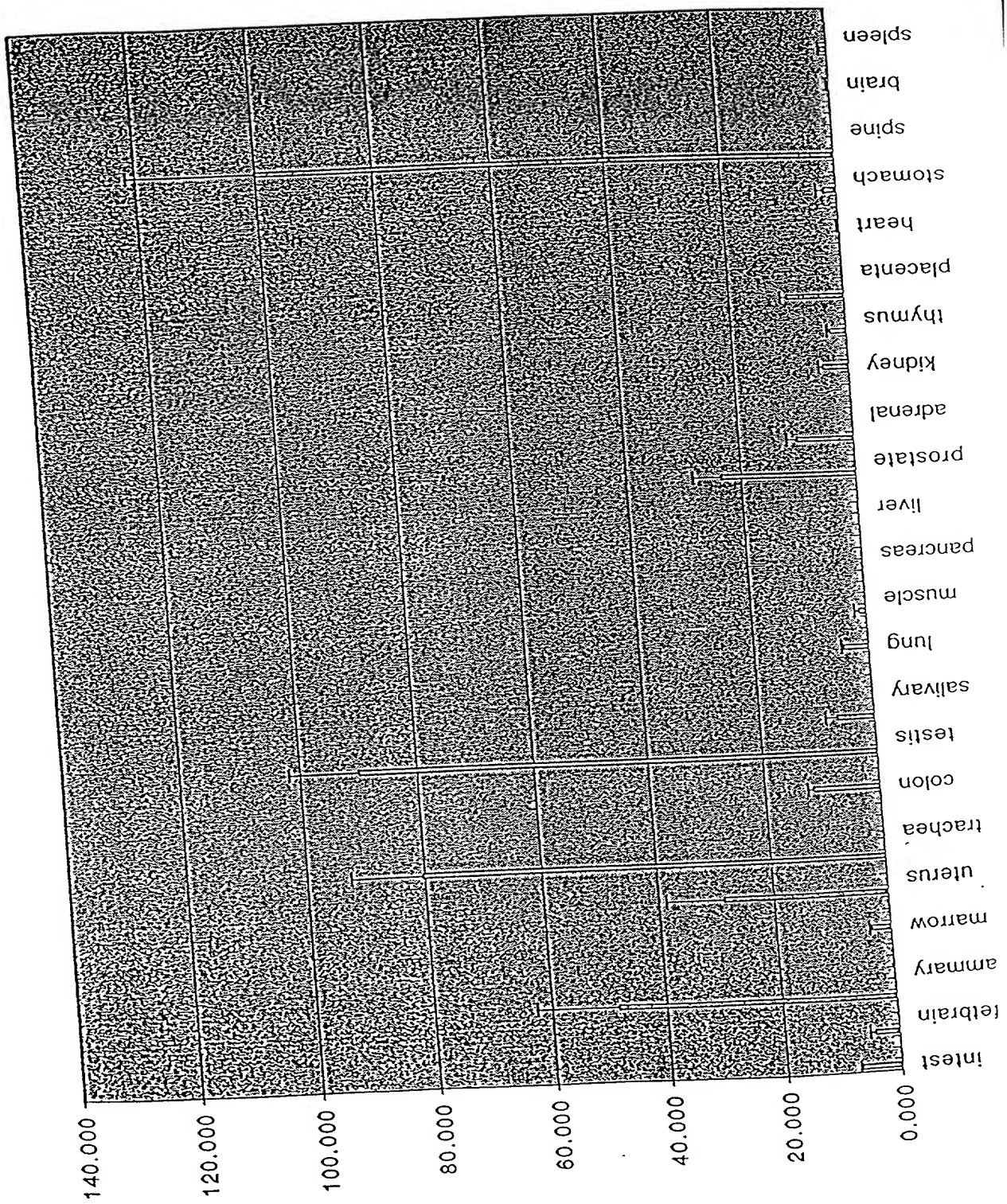


FIGURE 21

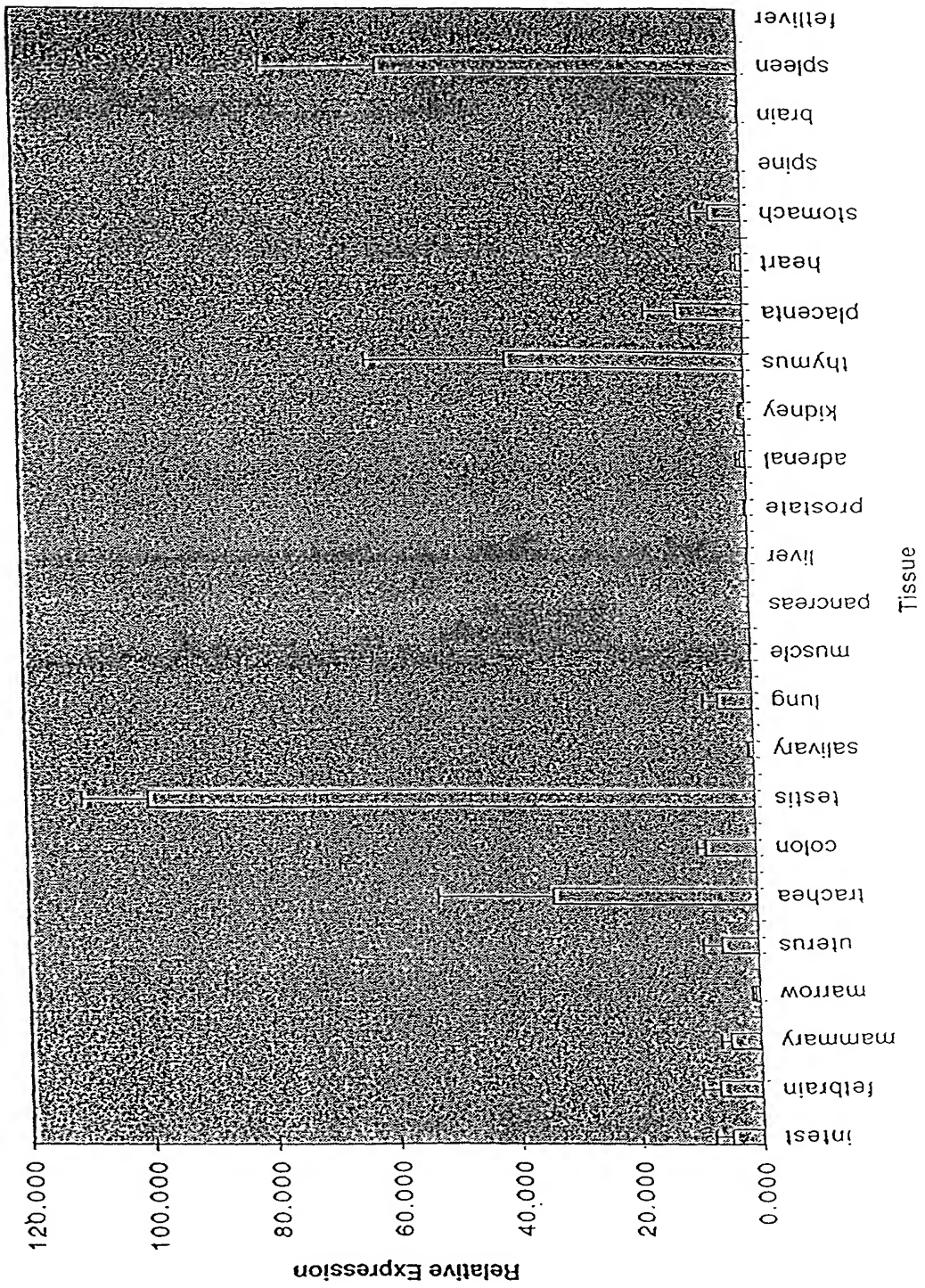

IL17C Distribution
Relative Expression
120.000
100.000
80.000
60.000
40.000
20.000
0.000
Tissue
intest
fetbrain
mammary
marrow
uterus
trachea
colon
testis
salivary
lung
muscle
pancreas
liver
prostate
adrenal
kidney
thymus
placenta
heart
stomach
spine
brain
spleen
fetliver

FIGURE 22

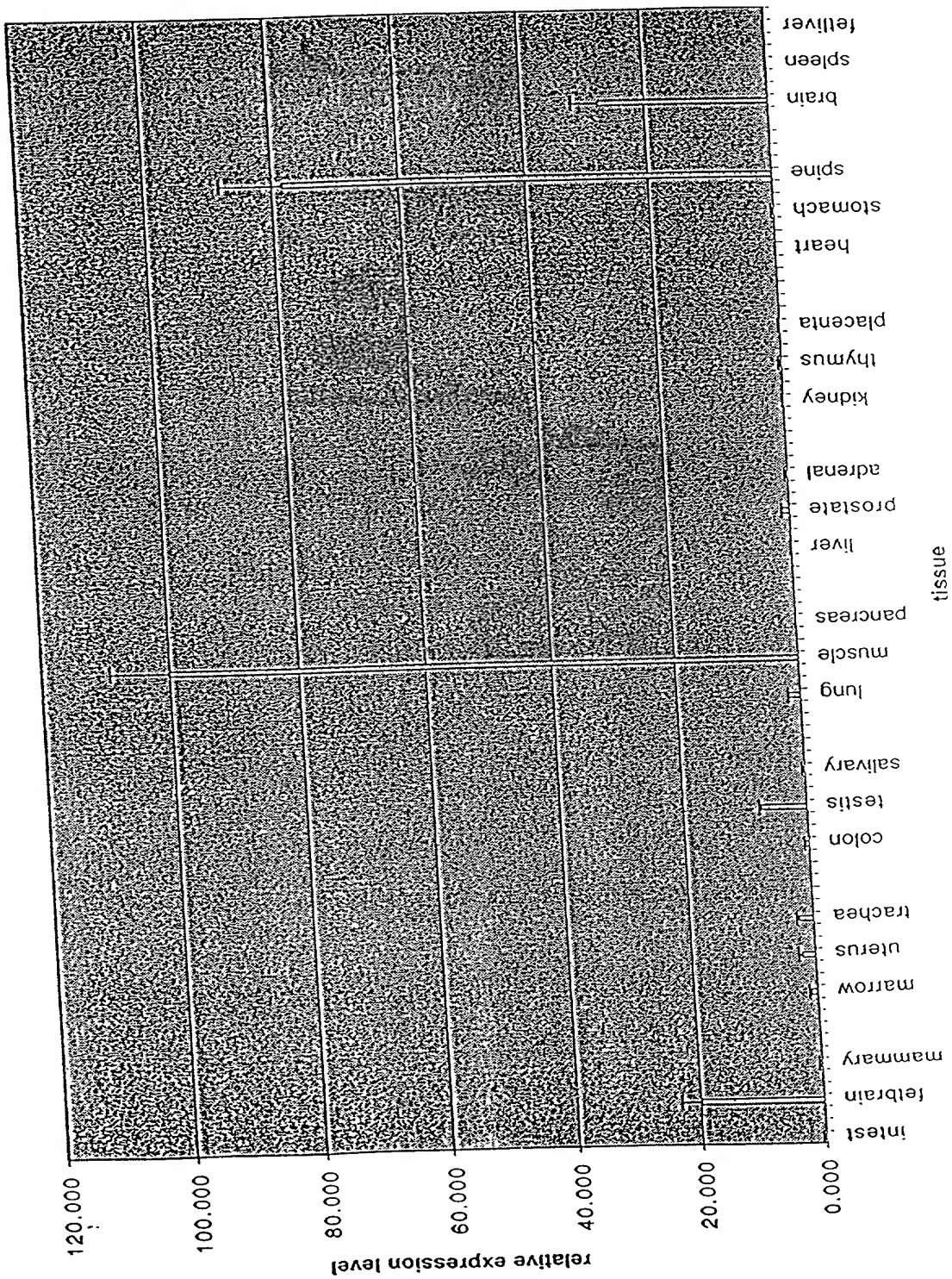

IL17D Distribution
relative expression level
0.000
20.000
40.000
60.000
80.000
100.000
120.000
intest
fetbrain
mammary
marrow
uterus
trachea
colon
testis
salivary
lung
muscle
pancreas
liver
prostate
adrenal
kidney
thymus
placenta
heart
stomach
spine
brain
spleen
fetliver
tissue

FIGURE 23

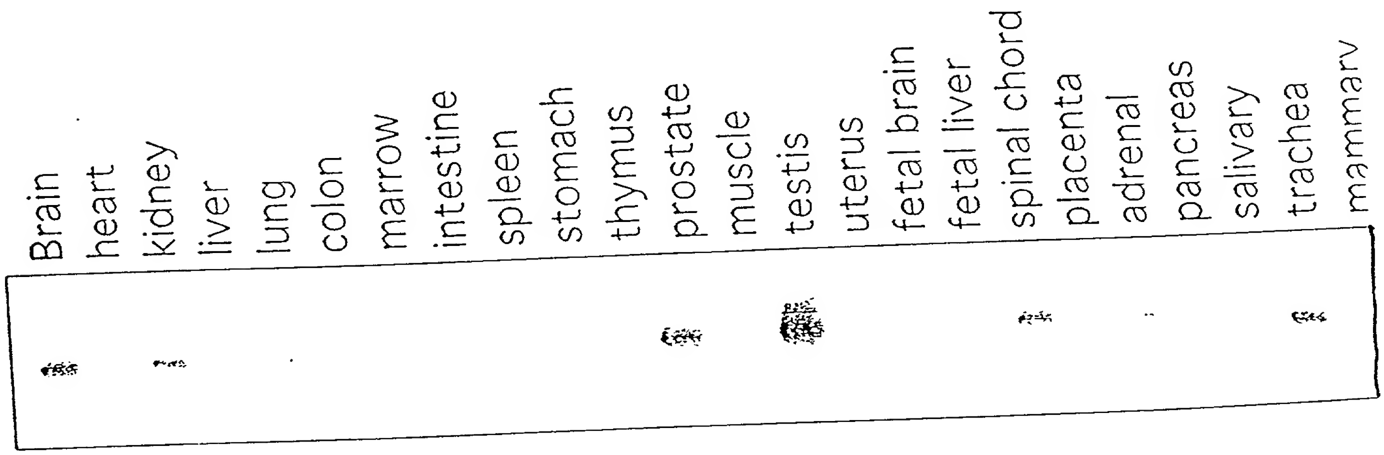

Brain
heart
kidney
liver
lung
colon
marrow
intestine
spleen
stomach
thymus
prostate
muscle
testis
uterus
fetal brain
fetal liver
spinal chord
placenta
adrenal
pancreas
salivary
trachea
mammary

FIGURE 24

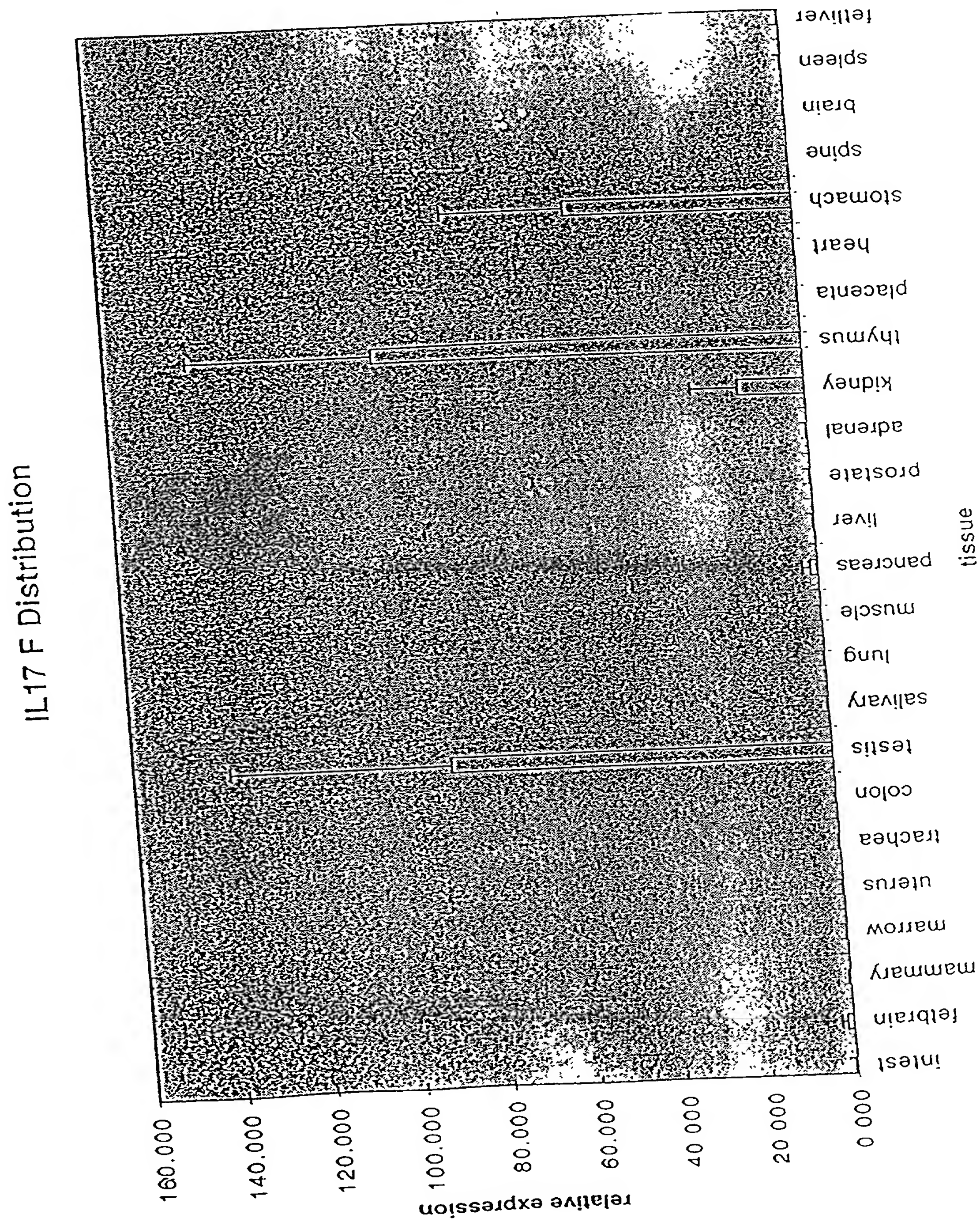

IL17 F Distribution
relative expression
160.000
140.000
120.000
100.000
80.000
60.000
40.000
20.000
0.000
tissue
intest
fetbrain
mammary
marrow
uterus
trachea
colon
testis
salivary
lung
muscle
pancreas
liver
prostate
adrenal
kidney
thymus
placenta
heart
stomach
spine
brain
spleen
fetliver

FIGURE 25

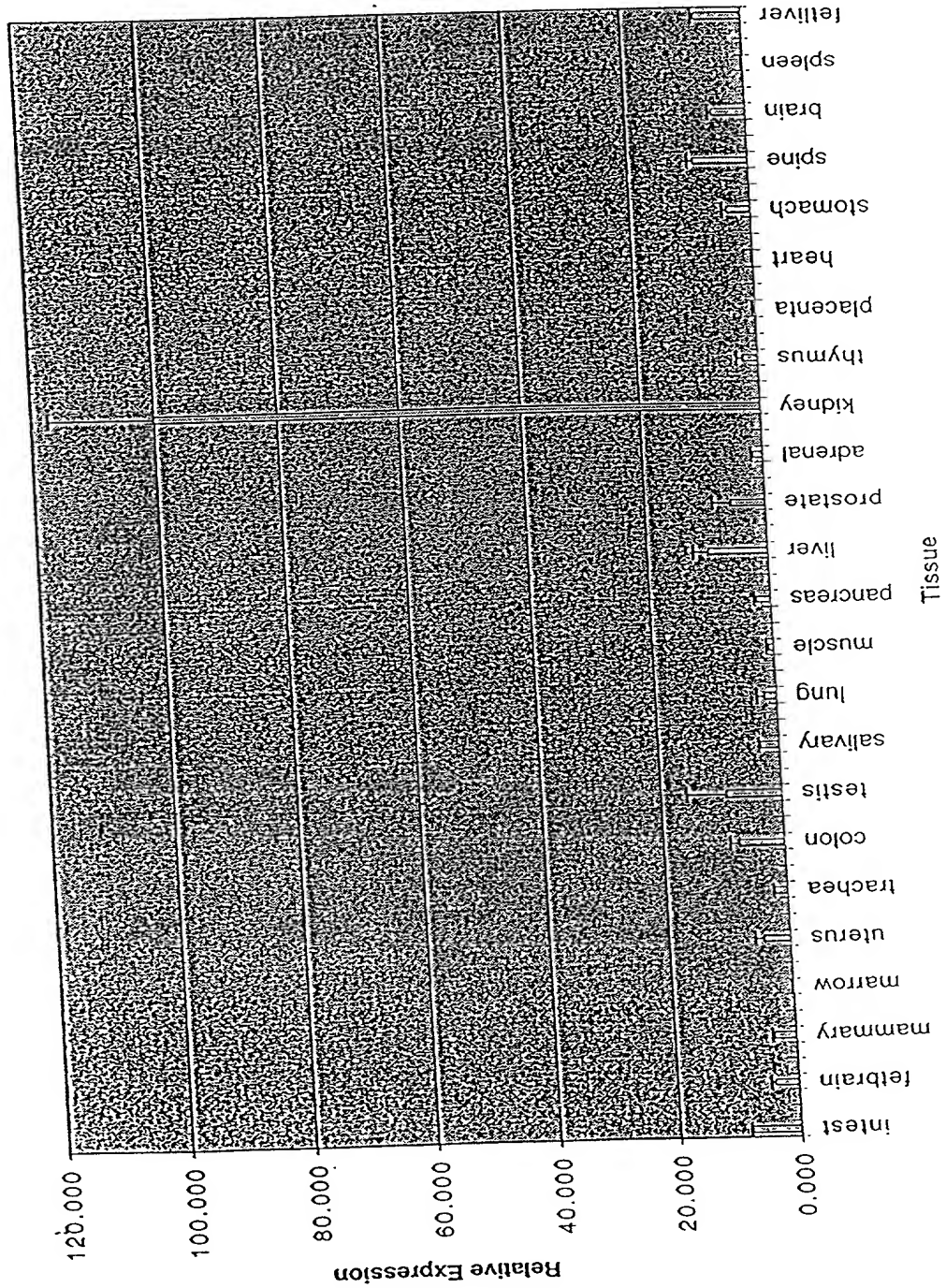

IL17Rhom-1 Distribution
Relative Expression
120.000
100.000
80.000
60.000
40.000
20.000
0.000
Tissue
liver
spleen
brain
spine
stomach
heart
placenta
thymus
kidney
adrenal
prostate
pancreas
liver
muscle
lung
salivary
testis
colon
trachea
uterus
marrow
mammary
fetbrain
intest

FIGURE 26

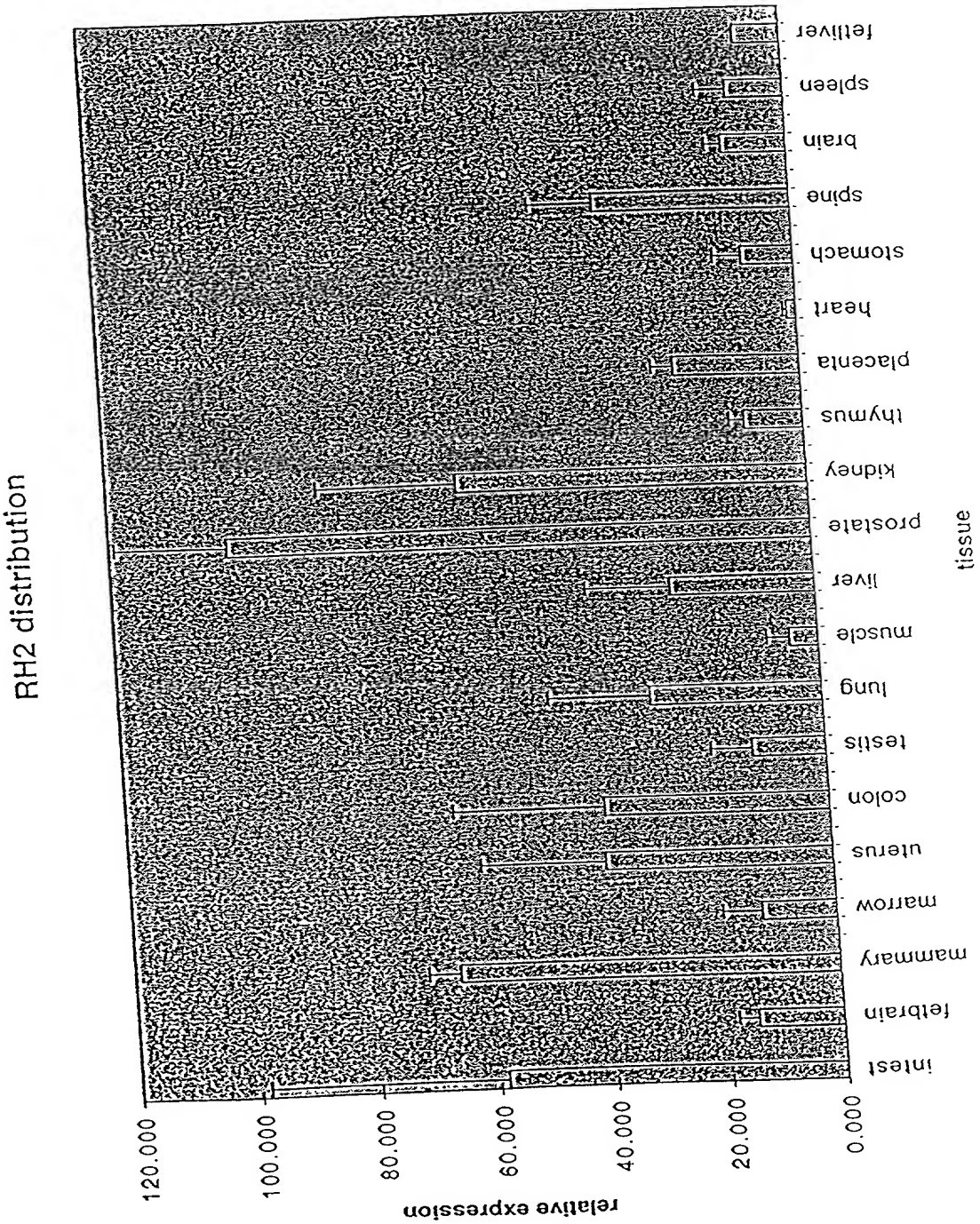

RH2 distribution
relative expression
120.000
100.000
80.000
60.000
40.000
20.000
0.000
tissue
intest
fetbrain
mammary
marrow
uterus
colon
testis
lung
muscle
liver
prostate
kidney
thymus
placenta
heart
stomach
spine
brain
spleen
fetliver

FIGURE 27

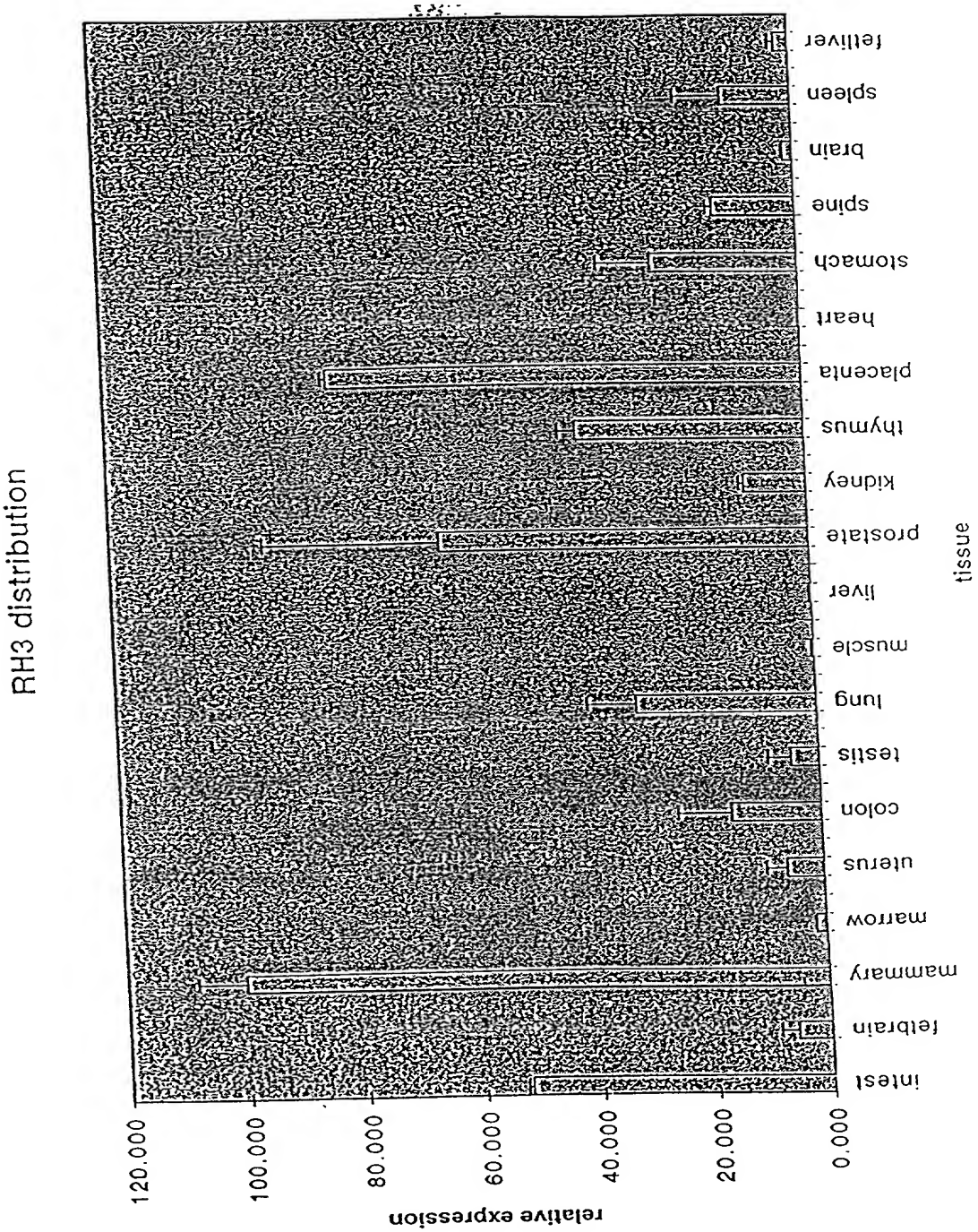

RH3 distribution
relative expression
120.000
100.000
80.000
60.000
40.000
20.000
0.000
tissue
intest
telbrain
mammary
marrow
uterus
colon
testis
lung
muscle
liver
prostate
kidney
thymus
placenta
heart
stomach
spine
brain
spleen
tellver

FIGURE 28

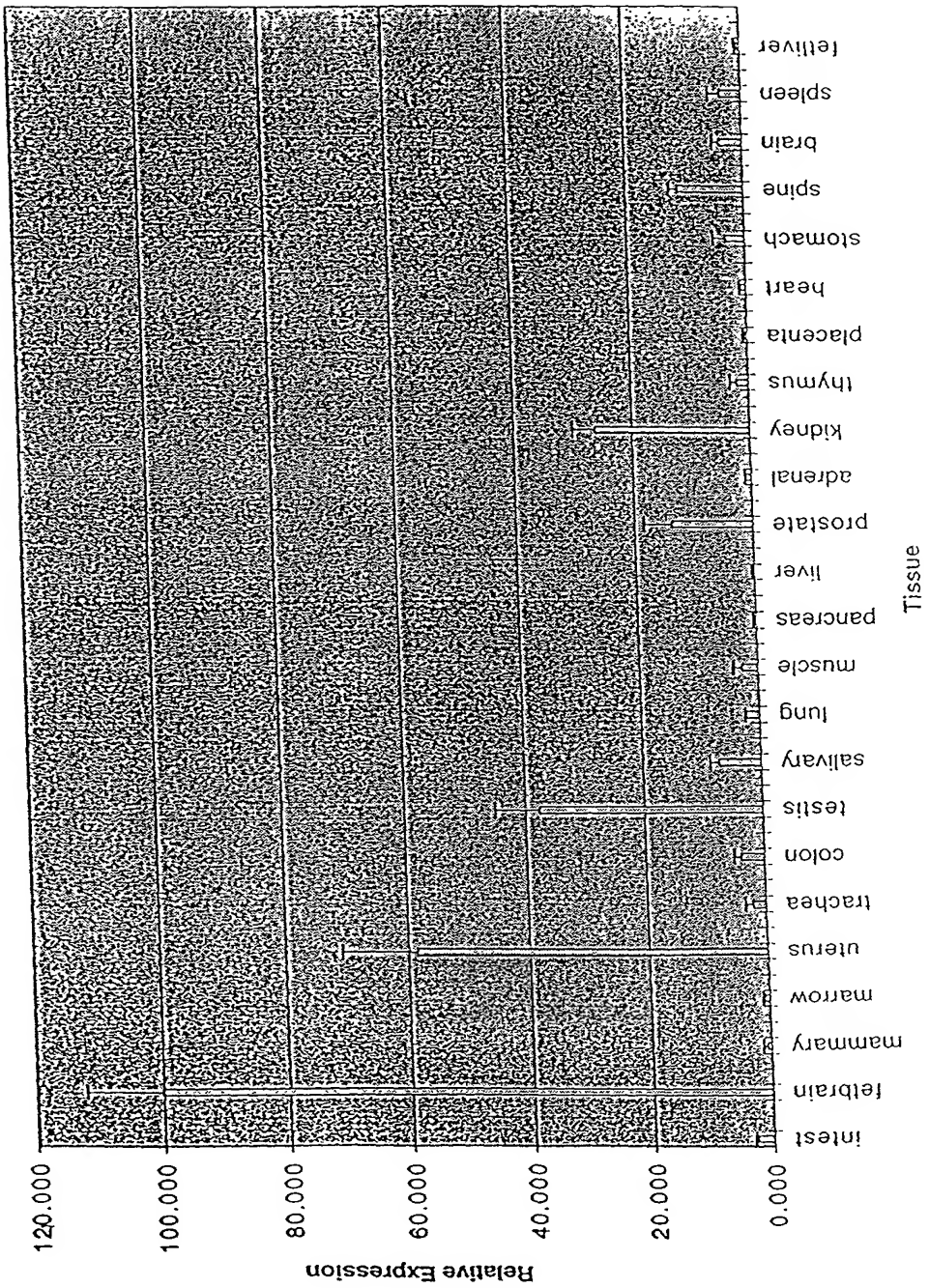

IL17 RH4 distribution
Relative Expression
120.000
100.000
80.000
60.000
40.000
20.000
0.000
Tissue
intest
fetbrain
mammary
marrow
uterus
trachea
colon
testis
saliva
lung
muscle
pancreas
liver
prostate
adrenal
kidney
thymus
placenta
heart
stomach
spine
brain
spleen
fetliver

FIGURE 29

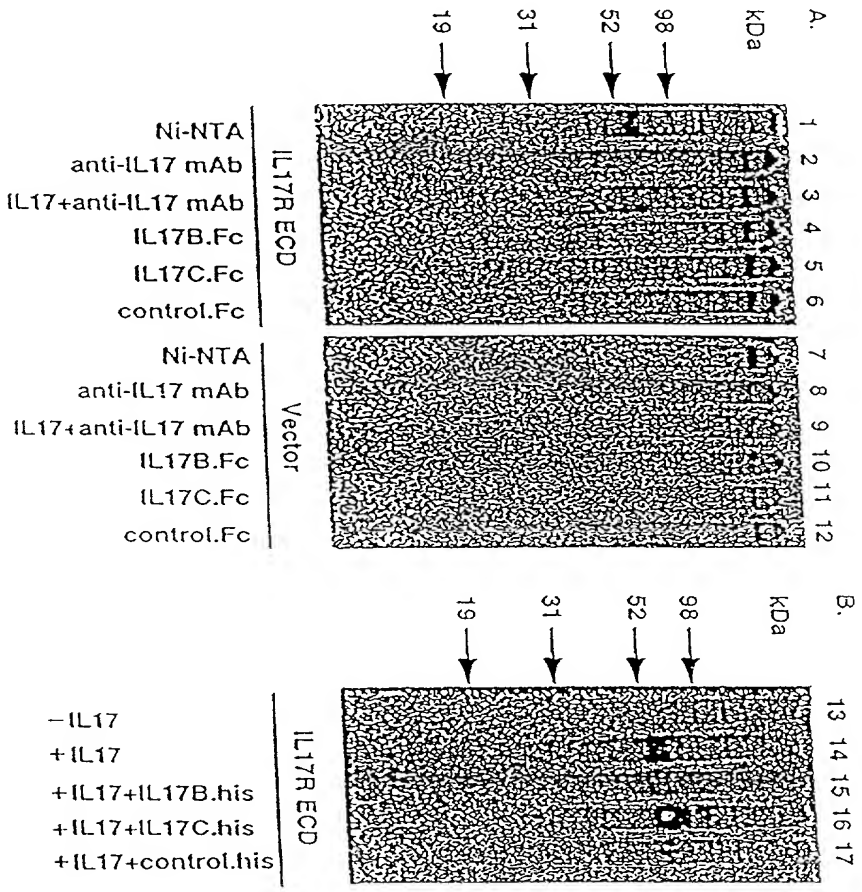

A.
kDa
19
31
52
98
1 2 3 4 5 6
Ni-NTA
anti-IL17 mAb
IL17+anti-IL17 mAb
IL17B.Fc
IL17C.Fc
control.Fc
IL17R ECD
7 8 9 10 11 12
Ni-NTA
anti-IL17 mAb
IL17+anti-IL17 mAb
IL17B.Fc
IL17C.Fc
control.Fc
Vector
B.
kDa
19
31
52
98
13 14 15 16 17
-IL17
+IL17
+IL17+IL17B.his
+IL17+IL17C.his
+IL17+control.his
IL17R ECD

FIGURE 30

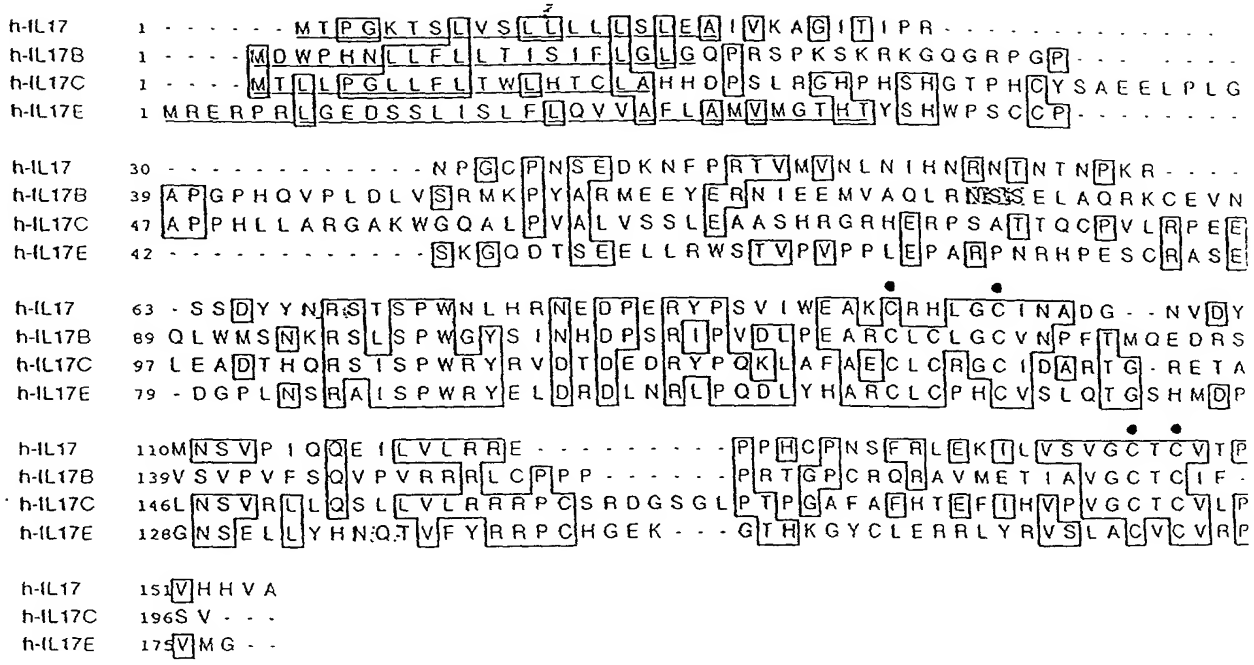

h-IL17 1 - - - - - - MTPGKTSLVSLLLLLSLEAIVKAGITIPR - - - - - - - - - - - - -
h-IL17B 1 - - - - MDWPHNLLFLLTISIFLGLGQPRSPKSKRKGQGRPGP - - - - - - - -
h-IL17C 1 - - - - MTLLPGLLFLTWLHTCLAHHDPSLRGHPHSHGTPHCYSAEELPLG
h-IL17E 1 MRERPRLGEDSSLISLFLQVVAFLAMVMGTHTYSHWPSCCP - - - - - - - -
h-IL17 30 - - - - - - - - - - - - - NPGCPNSEDKNFPRTVMVNLNIHNRNTNTNPKR - - - -
h-IL17B 39 APGPHQVPLDLVSRMKPYARMEEYERNIEEMVAQLRNSSELAQRKCEVN
h-IL17C 47 APPHLLARGAKWGQALPVALVSSLEAASHRGRHERPSATTQCPVLRPEE
h-IL17E 42 - - - - - - - - - - - - SKGQDTSELLRWSTVPVPPLEPARPNRHPESCRASE
h-IL17 63 - SSDYYNRSTSPWNLHRNEDPERYPSVIWEAKCRHLGCINADG - - NVDY
h-IL17B 89 QLWMSNKRSLSPWGYSINHDPSRIPVDLPEARCLCLGCVNPFTMQEDRS
h-IL17C 97 LEADTHQRSTSPWRYRVDTDEDRYPQKLAFAECLCRGCIDARTG - RETA
h-IL17E 79 - DGPLNSRAISPWRYELDRDLNRLPQDLYHARCLCPHCVSLQTGSHMDP
h-IL17 110MNSVPIQQEILVLRREPPHCPNSFRLEKILVSVGCTCVTP
h-IL17B 139VSVPVFSQVPVRRALCPPP - - - - - - PRTGPCRQRAVMETIAVGCTCIF -
h-IL17C 146LNSVRLLQSLLVLARRPCSRDGSGLPTPGAFAFHTEFIHVPVGCTCVLP
h-IL17E 128GNSELLYHNQTVFYRRPCHGEK - - - GTHKGYCLERRLYRVSLACVCVRP
h-IL17 151VHHVA
h-IL17C 196SV - - -
h-IL17E 175VMG - -

FIGURE 31A

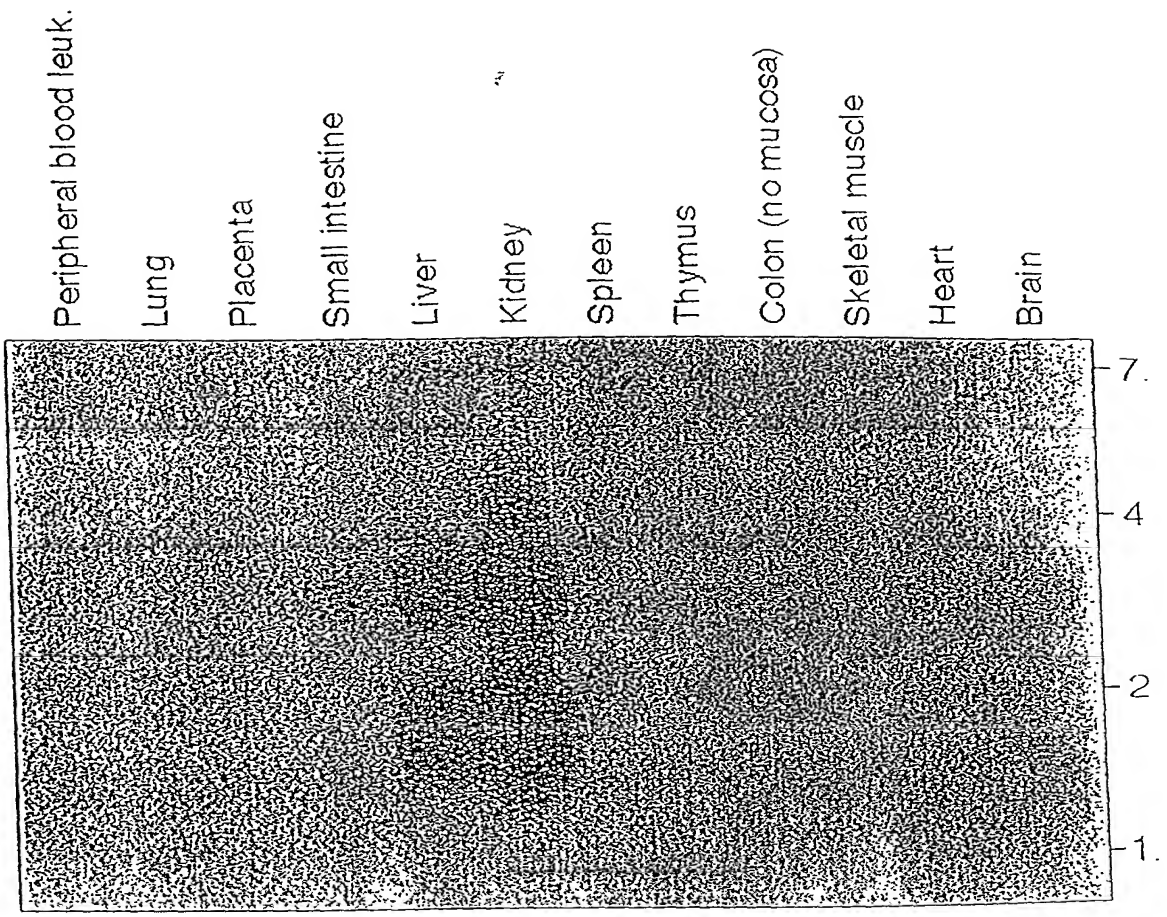


FIGURE 31B

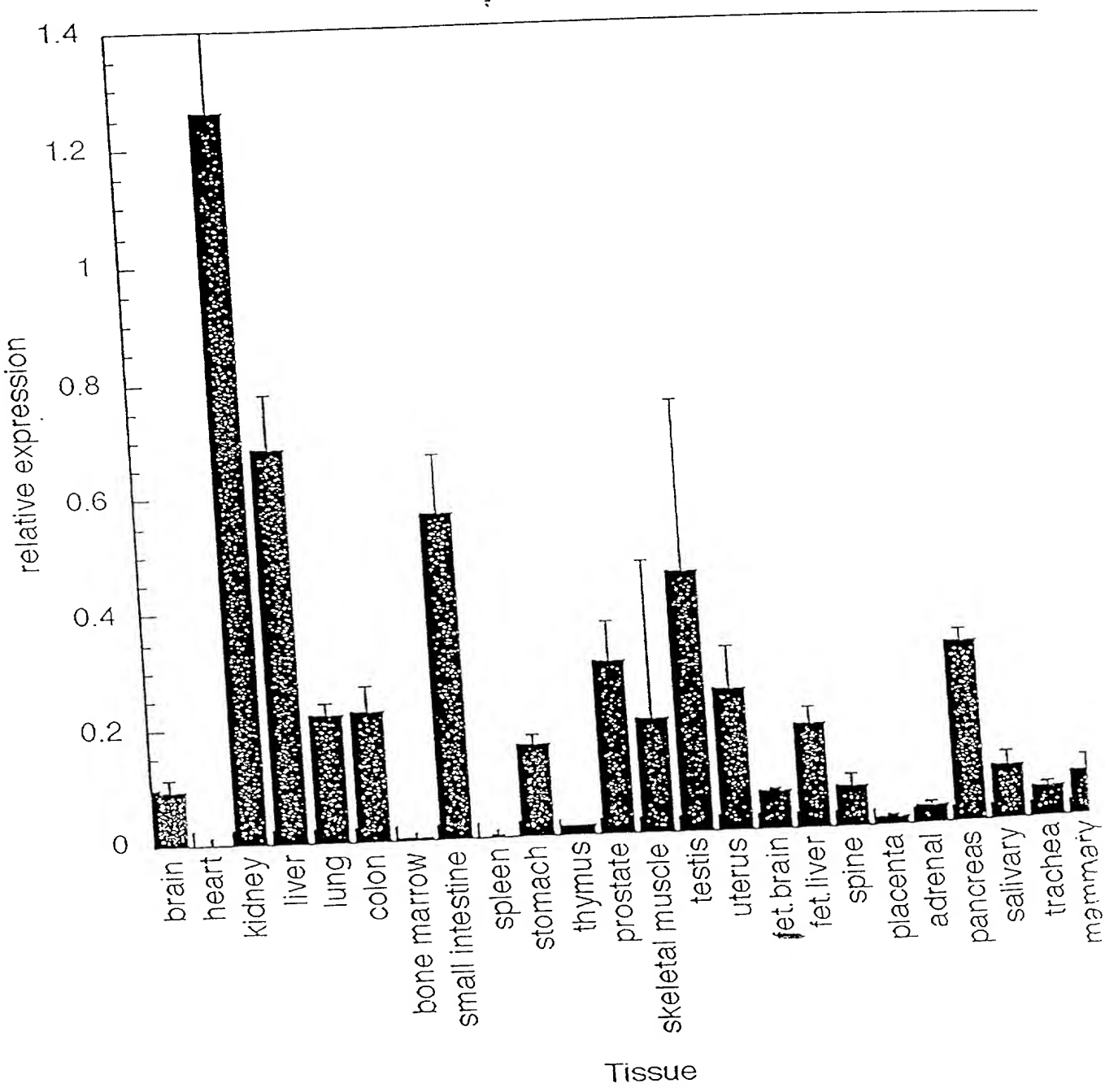
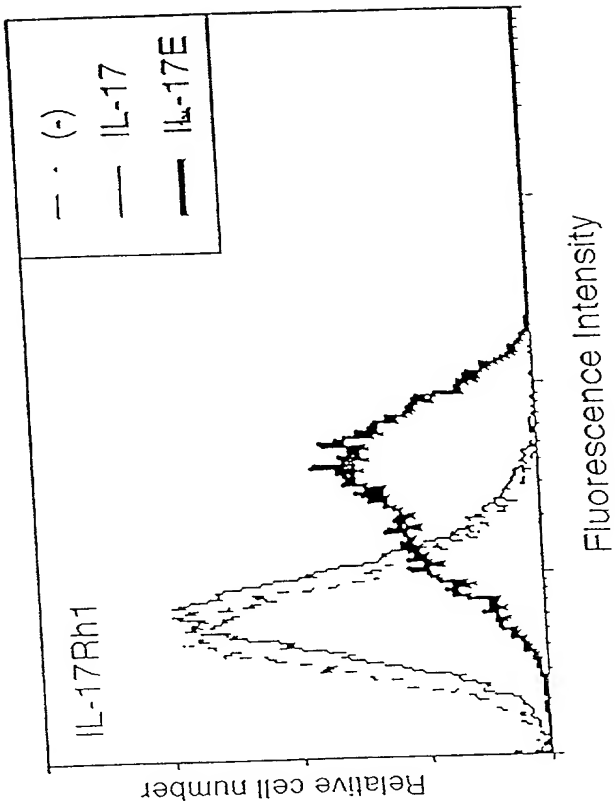

1.4
1.2
1
0.8
0.6
0.4
0.2
0
relative expression
brain
heart
kidney
liver
lung
colon
bone marrow
small intestine
spleen
stomach
thymus
prostate
skeletal muscle
testis
uterus
fet. brain
fet. liver
spine
placenta
adrenal
pancreas
salivary
trachea
mammary
Tissue

FIGURE 32A


IL-17Rh1
(-)
IL-17
IL-17E
Relative cell number
Fluorescence Intensity

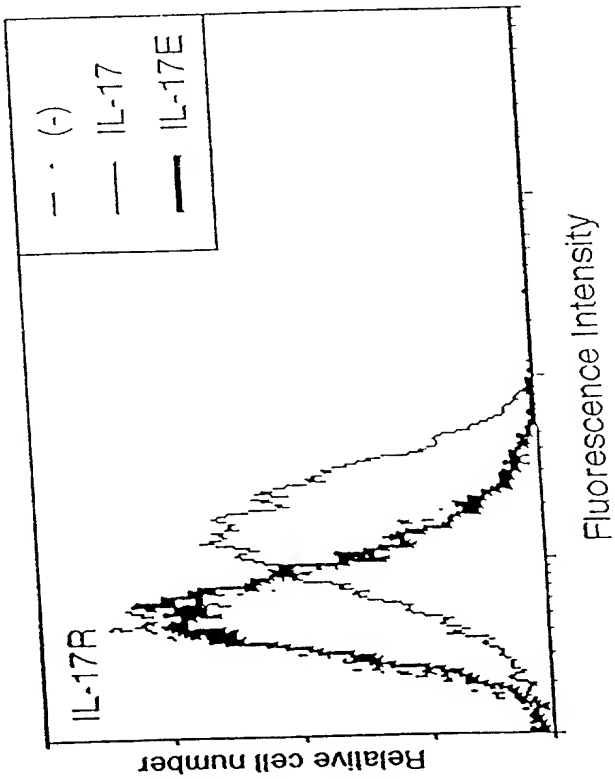

IL-17R
(-)
IL-17
IL-17E
Relative cell number
Fluorescence Intensity

FIGURE 32B

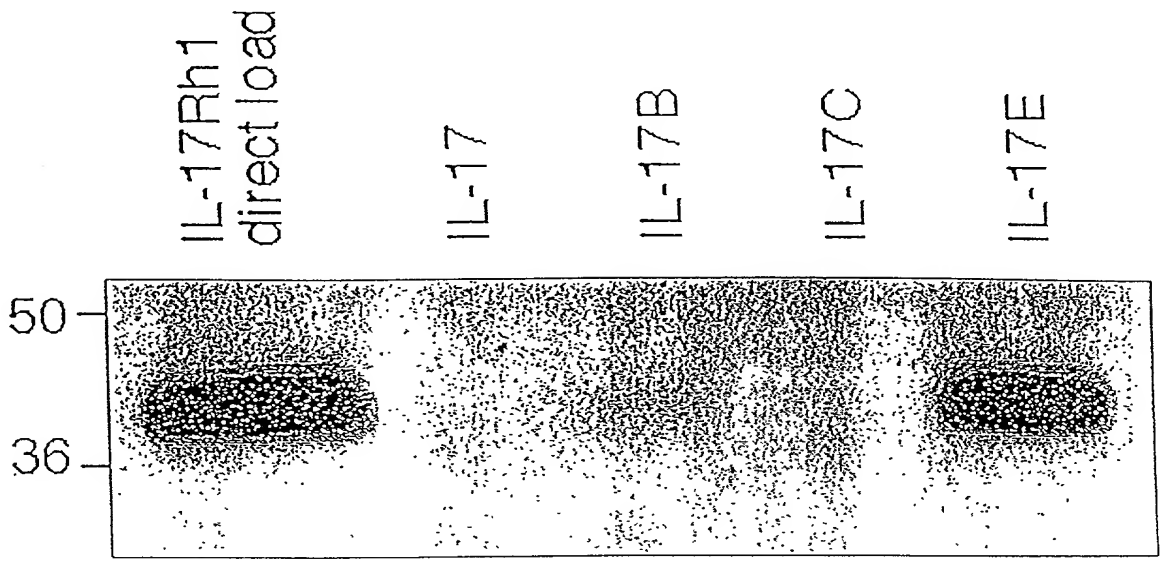


FIGURE 33

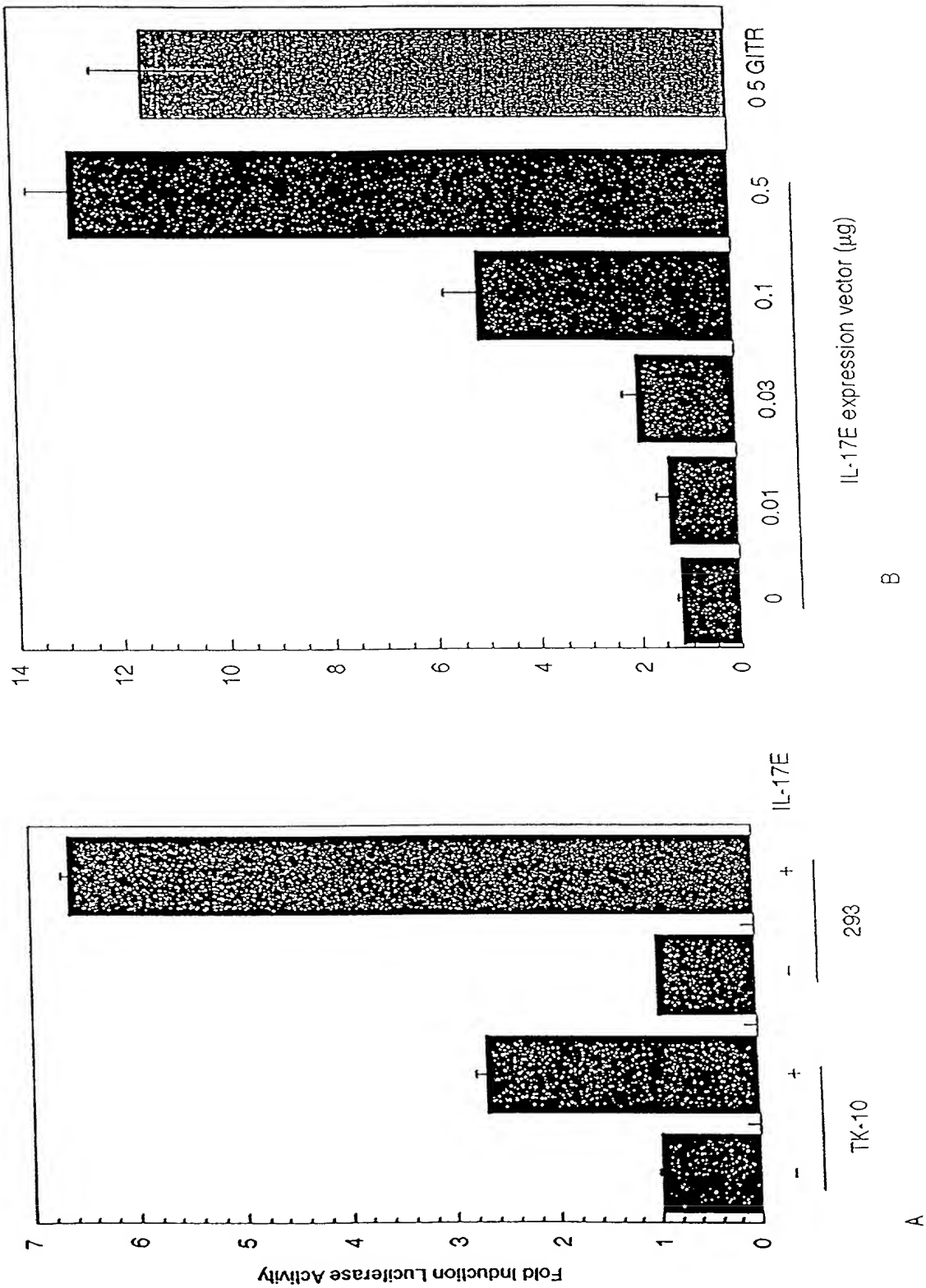
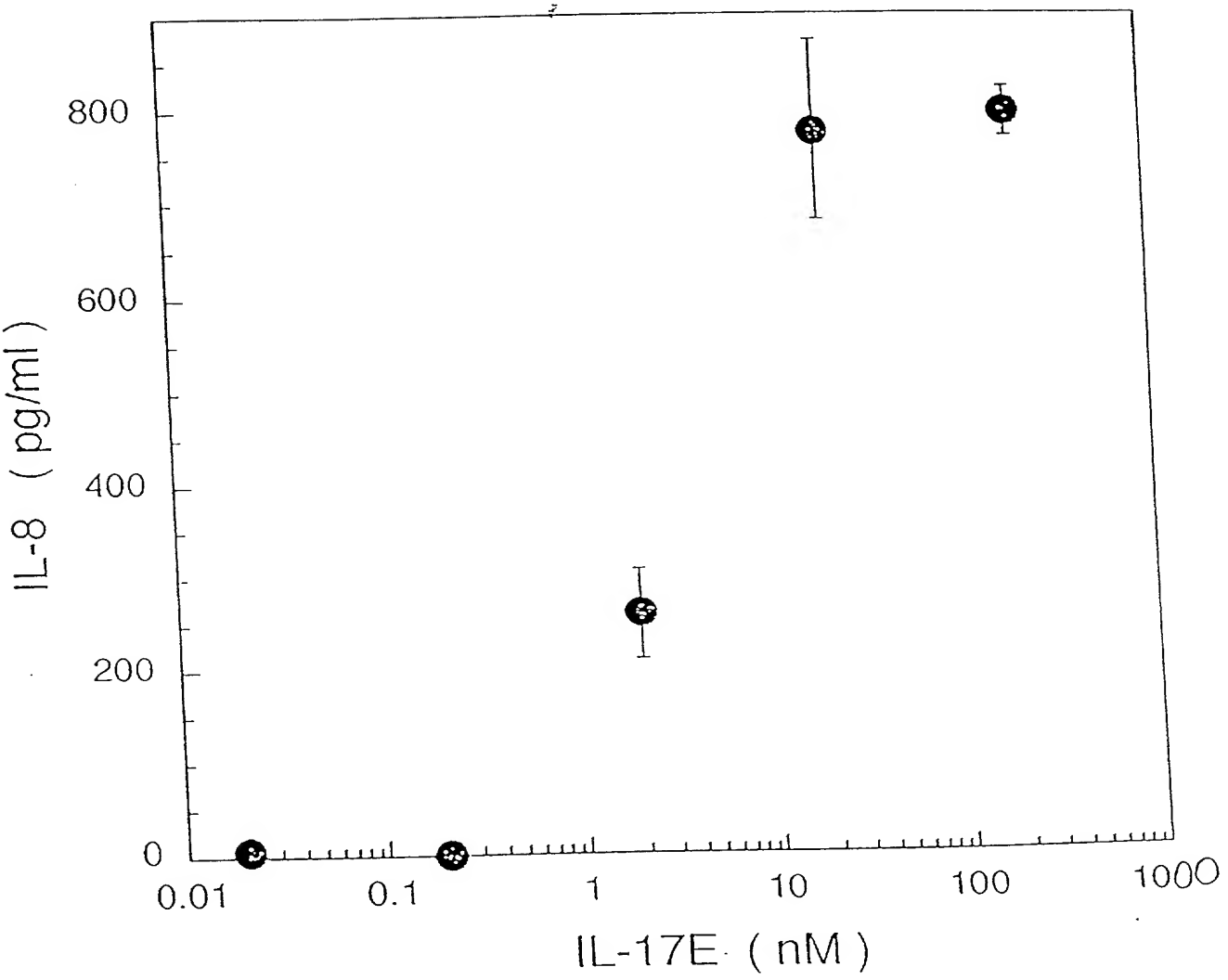

Fold Induction Luciferase Activity
0
1
2
3
4
5
6
7
TK-10
293
IL-17E
A
0
2
4
6
8
10
12
14
0
0.01
0.03
0.1
0.5
0.5 GITR
IL-17E expression vector (µg)
B

FIGURE 34



IL-17 family of cytokines has complex pattern of overlapping receptor-ligand specificities

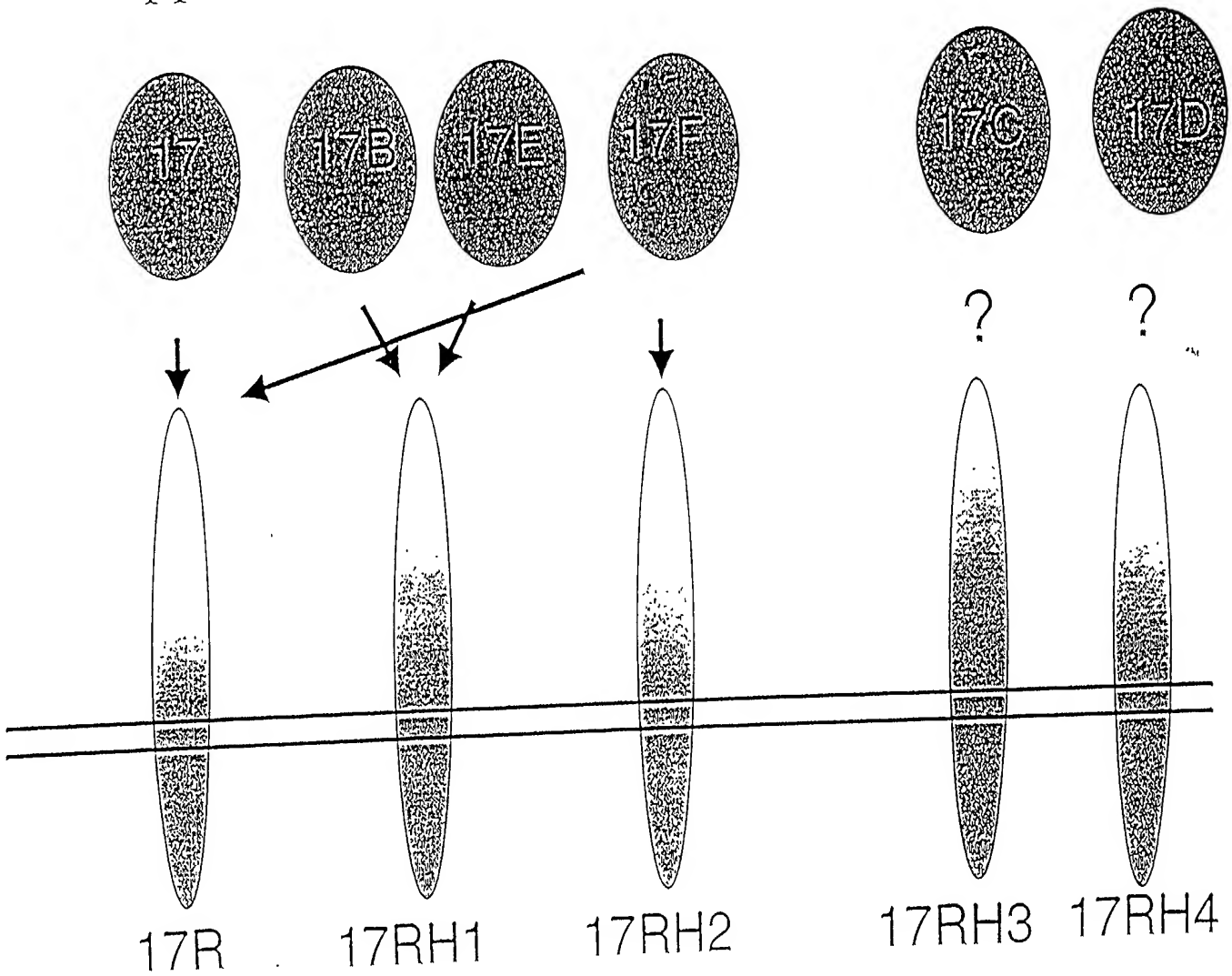
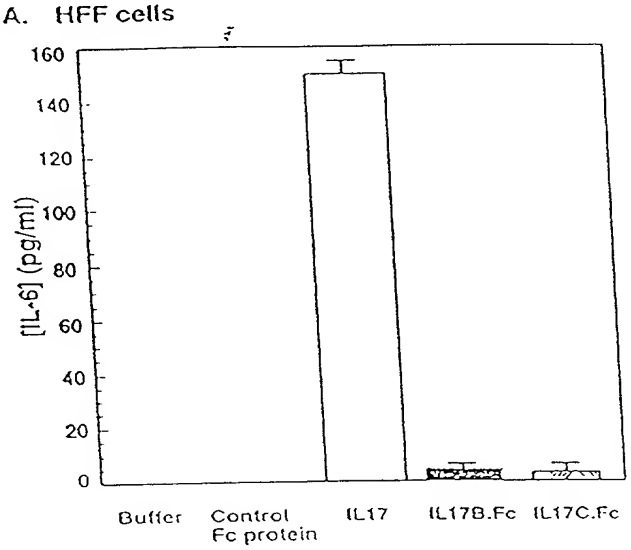


FIGURE 35

FIGURE 36

A. HFF cells



B. THP1 cells

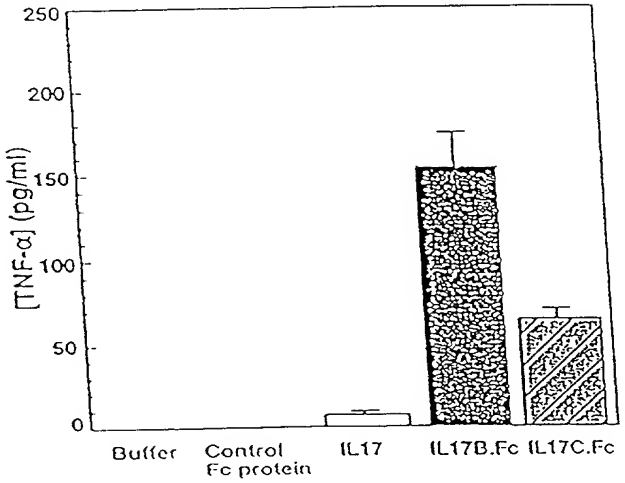


FIGURE 37

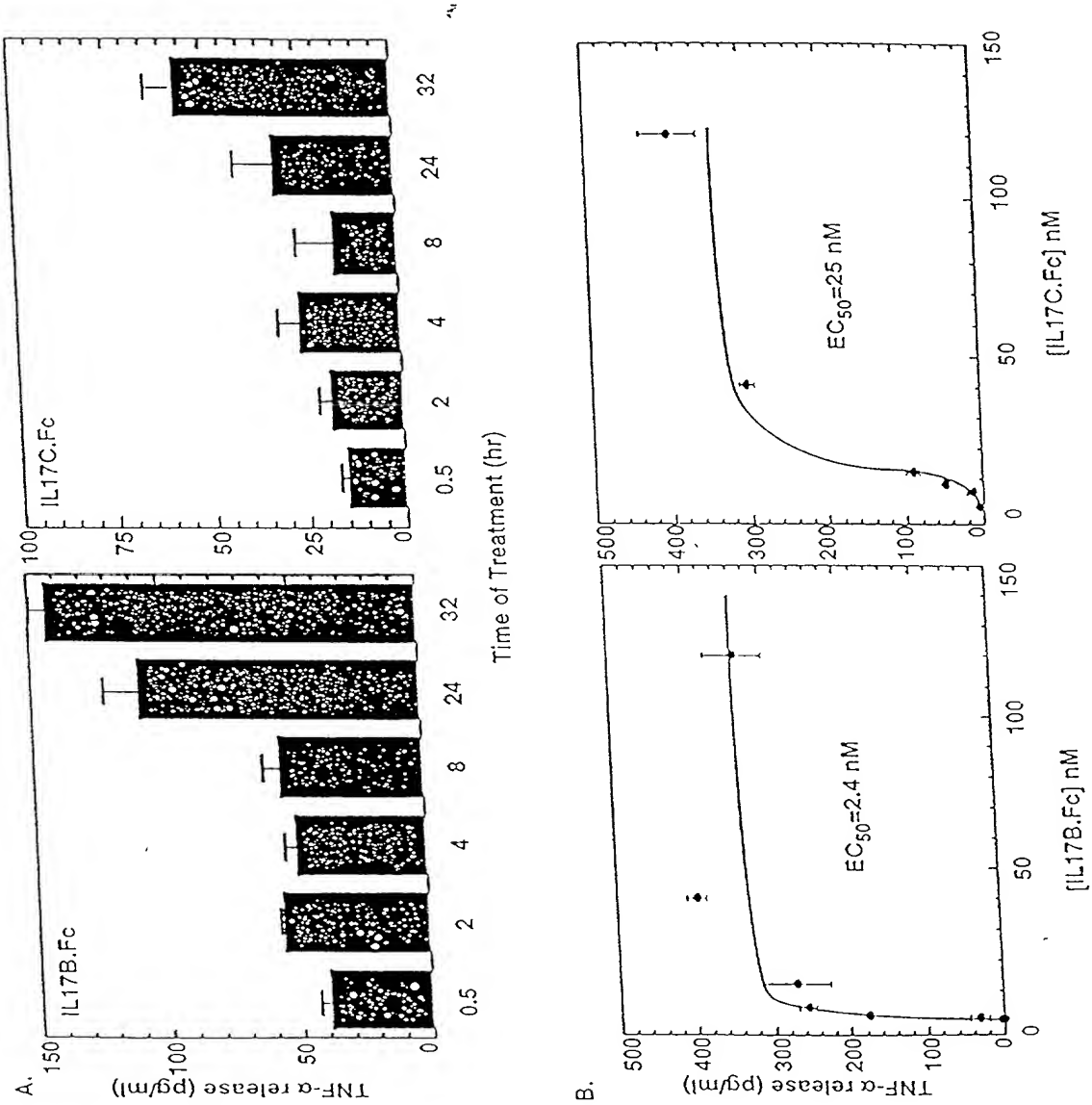

A.
IL17B.Fc
IL17C.Fc
TNF-α release (pg/ml)
Time of Treatment (hr)
0.5
2
4
8
24
32
B.
EC50=2.4 nM
EC50=25 nM
[IL17B.Fc] nM
[IL17C.Fc] nM

FIGURE 38

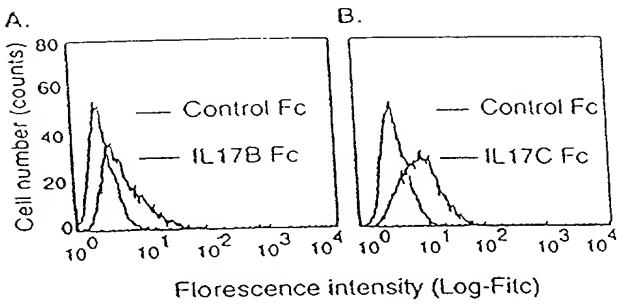


FIGURE 39

IL-17 induces breakdown and inhibits synthesis of cartilage matrix

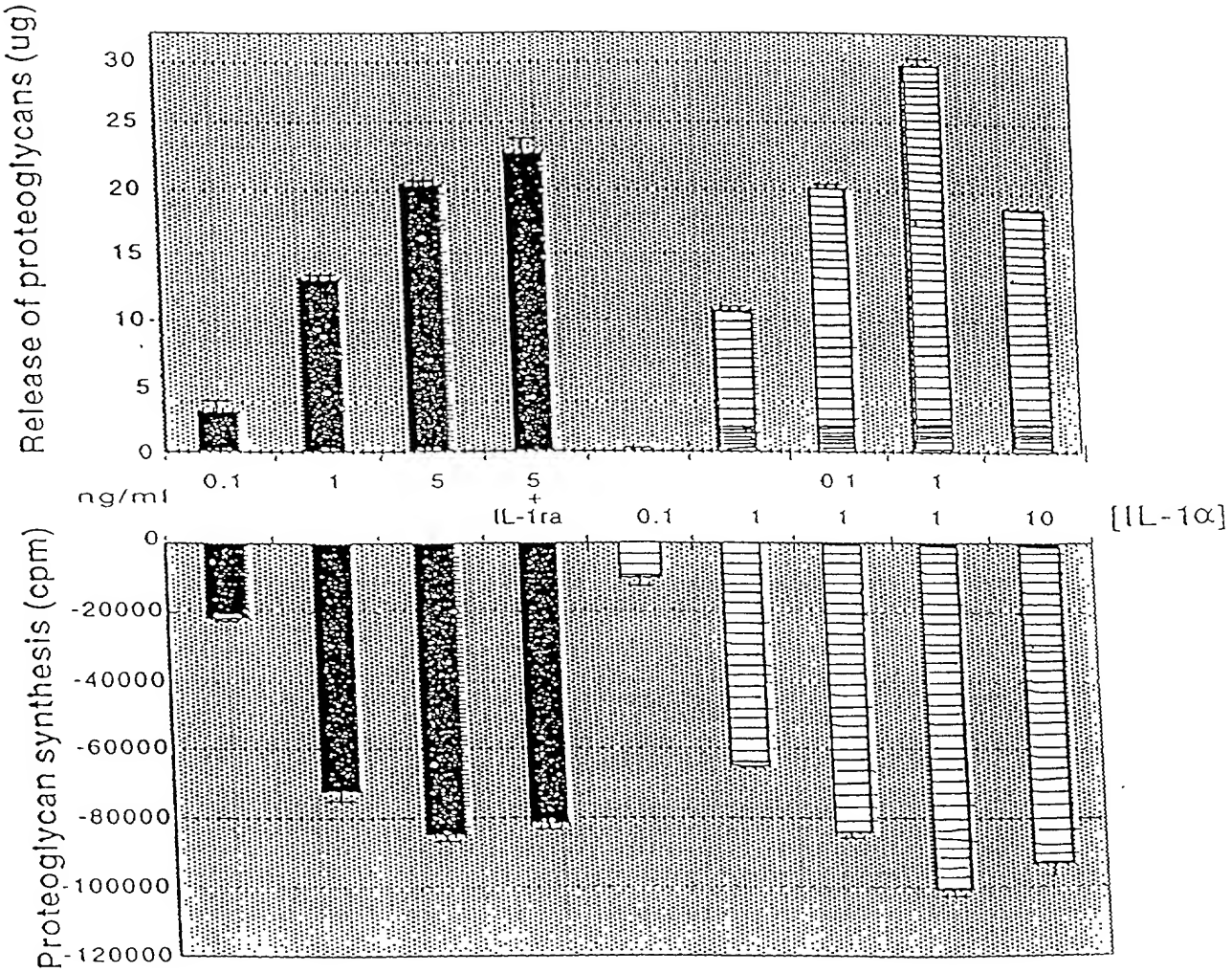


FIGURE 40

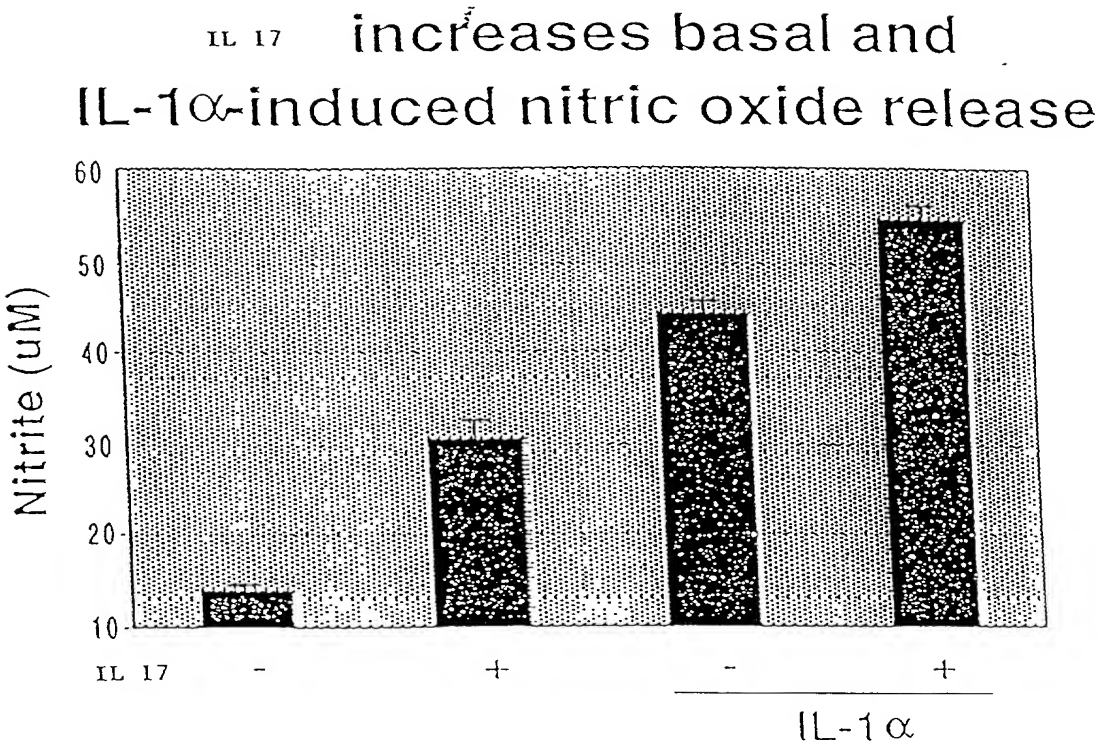

IL 17 increases basal and
IL-1α-induced nitric oxide release
Nitrite (uM)
60
50
40
30
20
10
IL 17 - + - +
IL-1α

FIGURE 41

Inhibition of nitric oxide release does not block the detrimental effects of IL-17 on matrix breakdown or synthesis

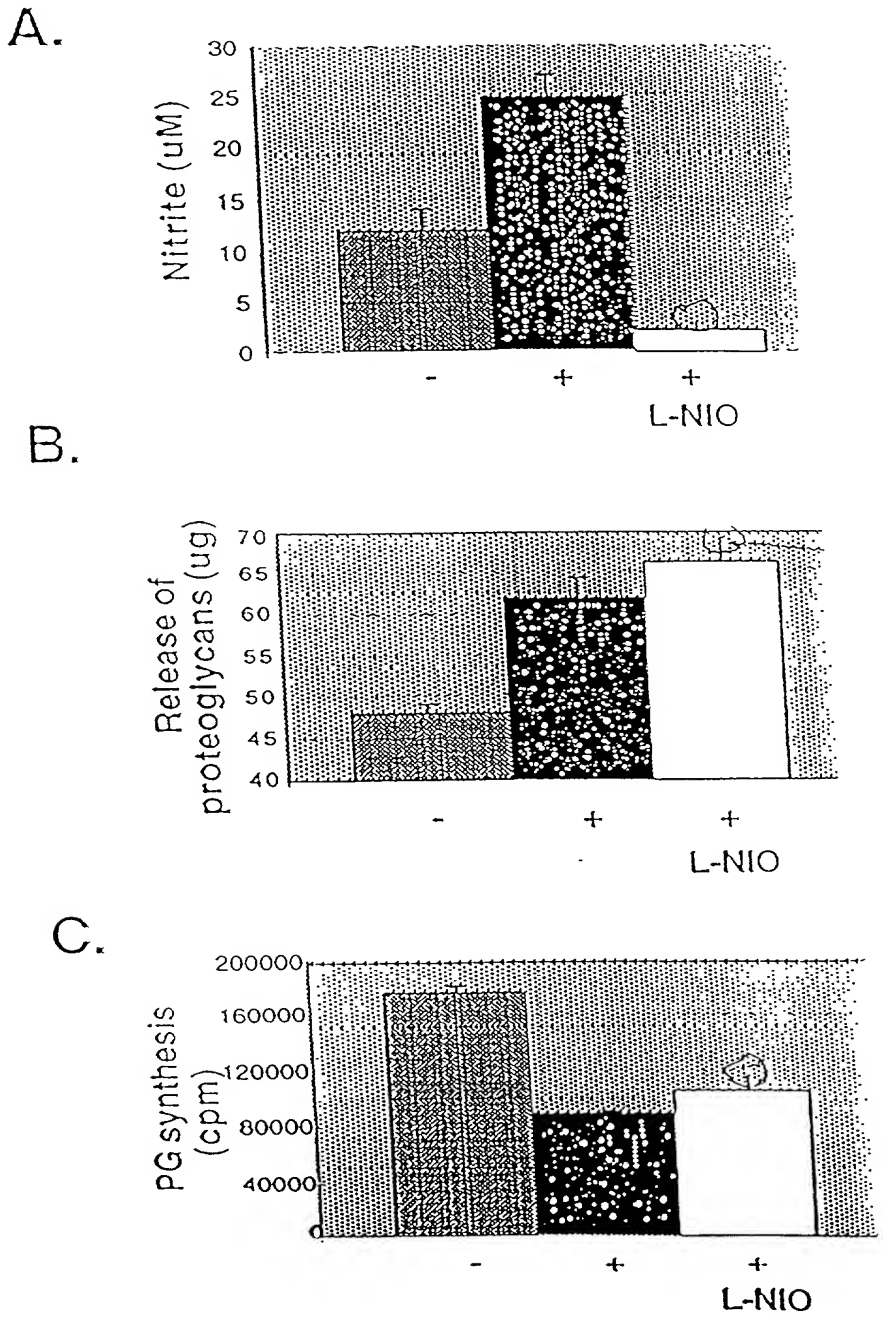


FIGURE 42

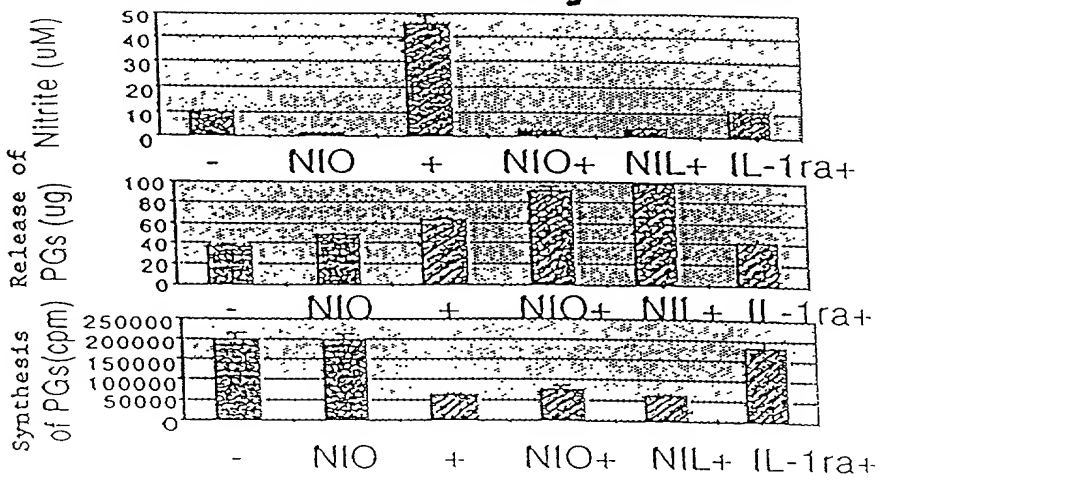


FIGURE 43

IL-17C

detrimental effects on articular cartilage

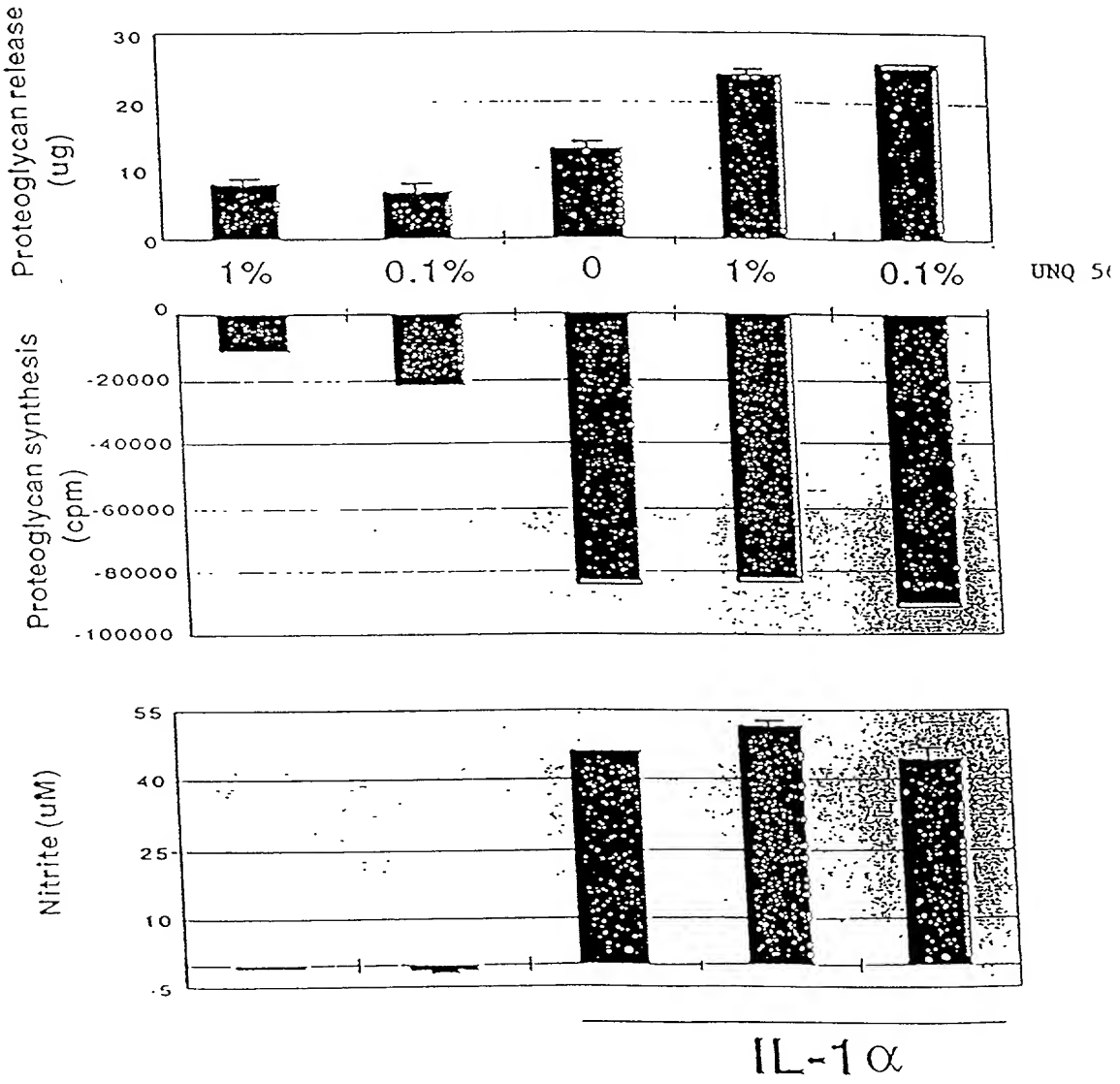


FIGURE 44

Inflammatory Bowel Disease: Expression of IL-17 Family in Mouse Model of IBD

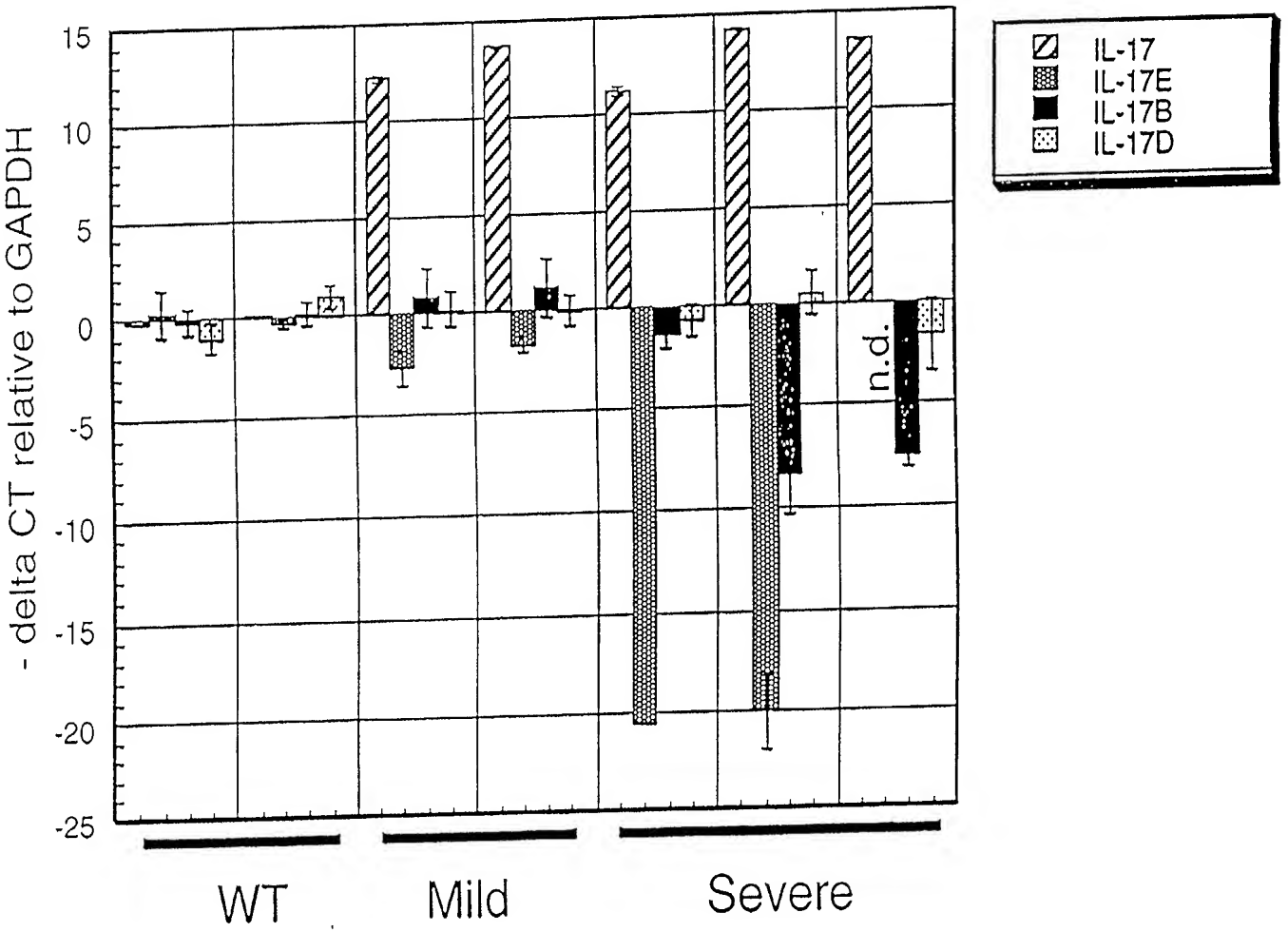


FIGURE 45

IL-17D, present in brain, decreases rapidly following stroke

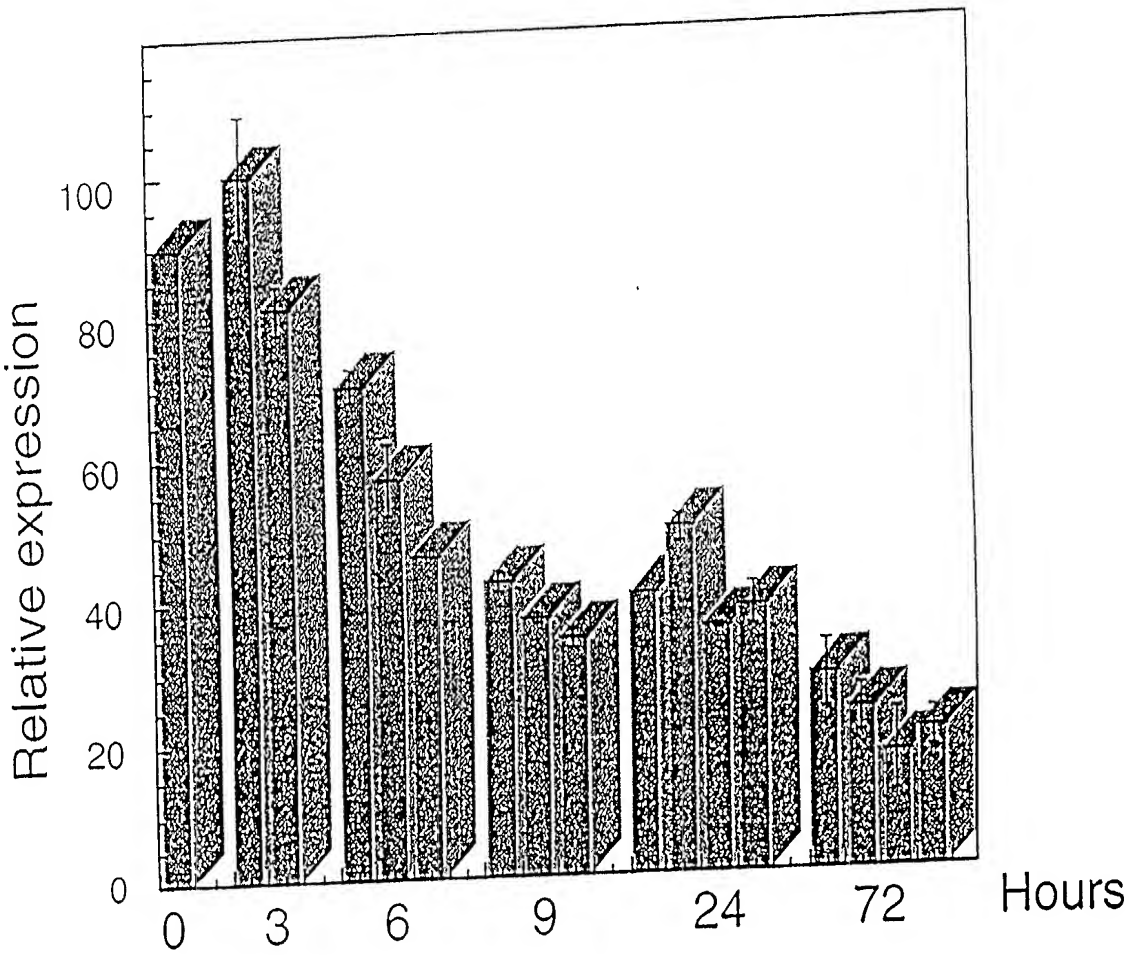


FIGURE 46

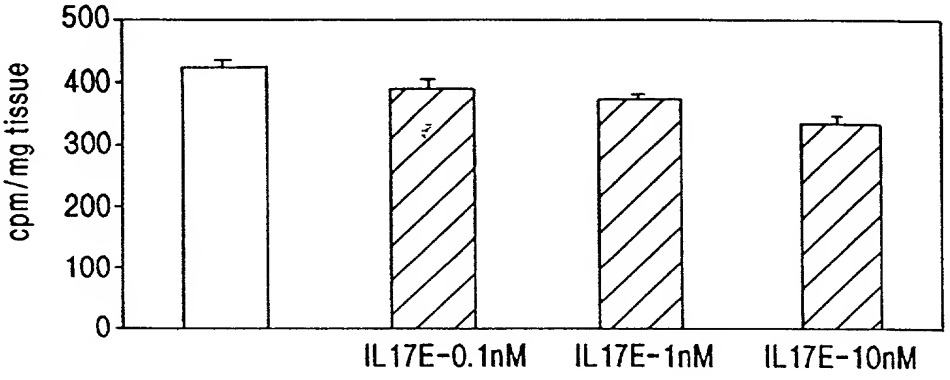


FIG. 46A

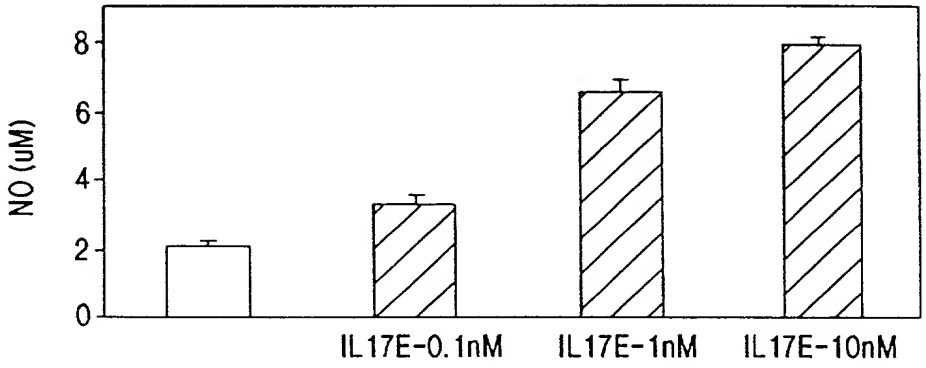


FIG. 46B

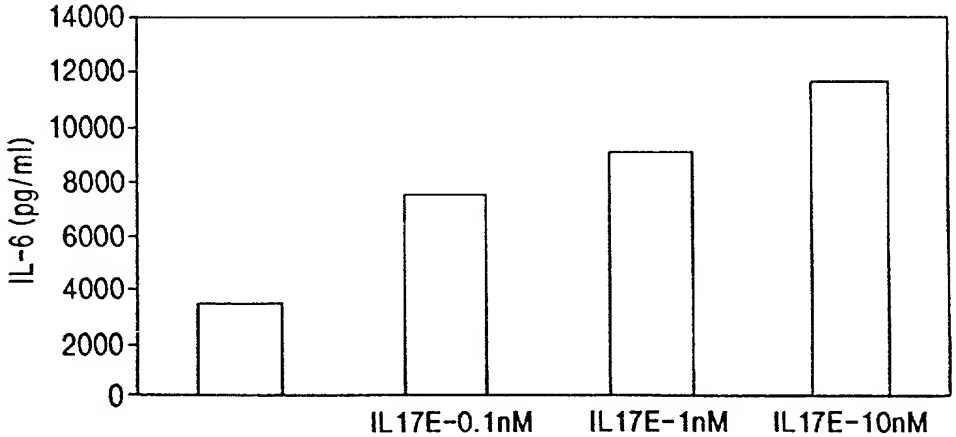


FIG. 46C

FIGURE 47

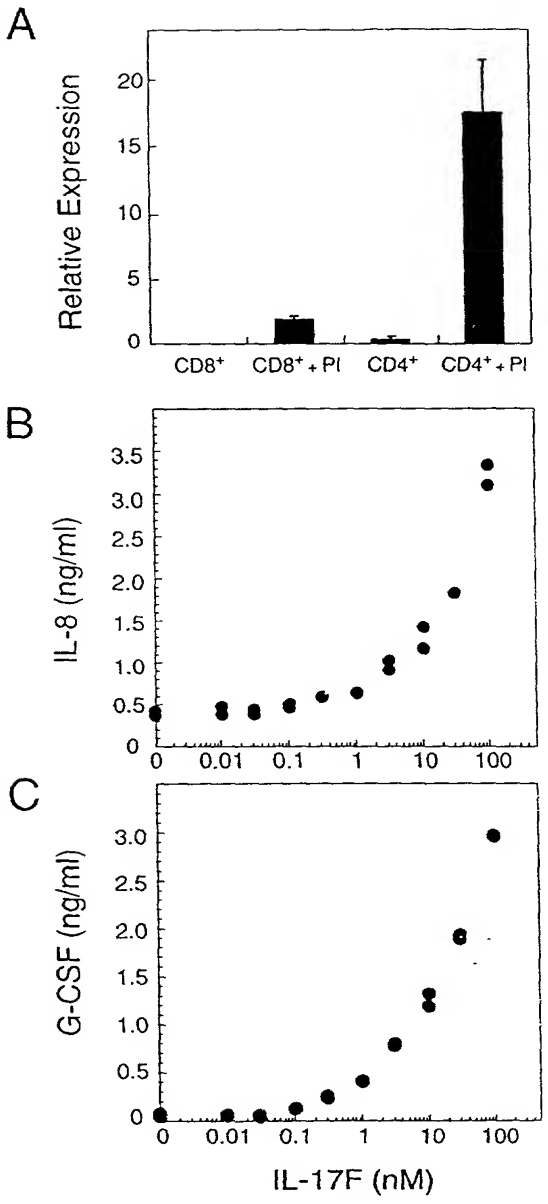

A
Relative Expression
20
15
10
5
0
CD8+
CD8+ + PI
CD4+
CD4+ + PI
B
IL-8 (ng/ml)
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0
0
0.01
0.1
1
10
100
C
G-CSF (ng/ml)
3.0
2.5
2.0
1.5
1.0
0.5
0
0
0.01
0.1
1
10
100
IL-17F (nM)

FIGURE 48

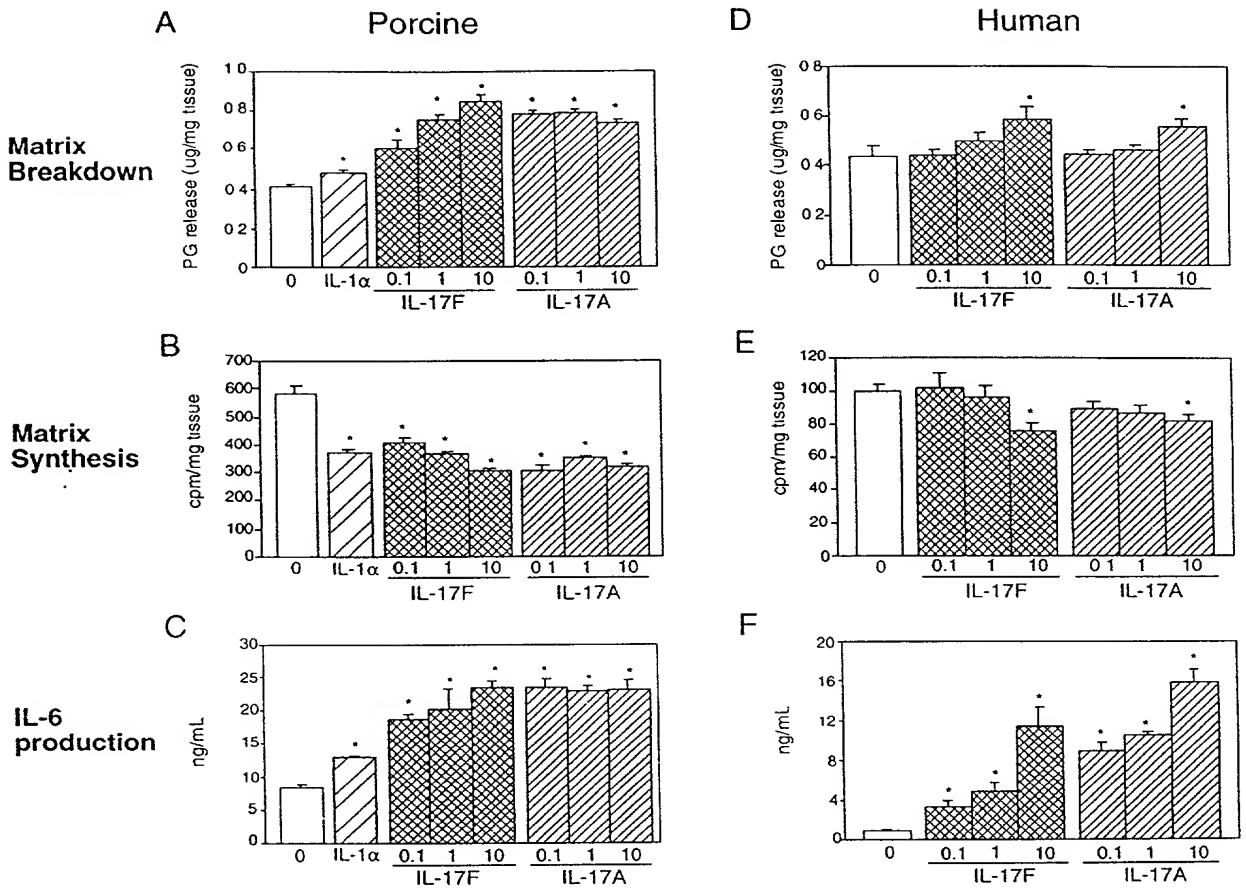

A
Porcine
D
Human
Matrix Breakdown
PG release (ug/mg tissue)
B
E
Matrix Synthesis
cpm/mg tissue
C
F
IL-6 production
ng/mL
0
IL-1α
0.1
1
10
IL-17F
IL-17A

FIGURE 49

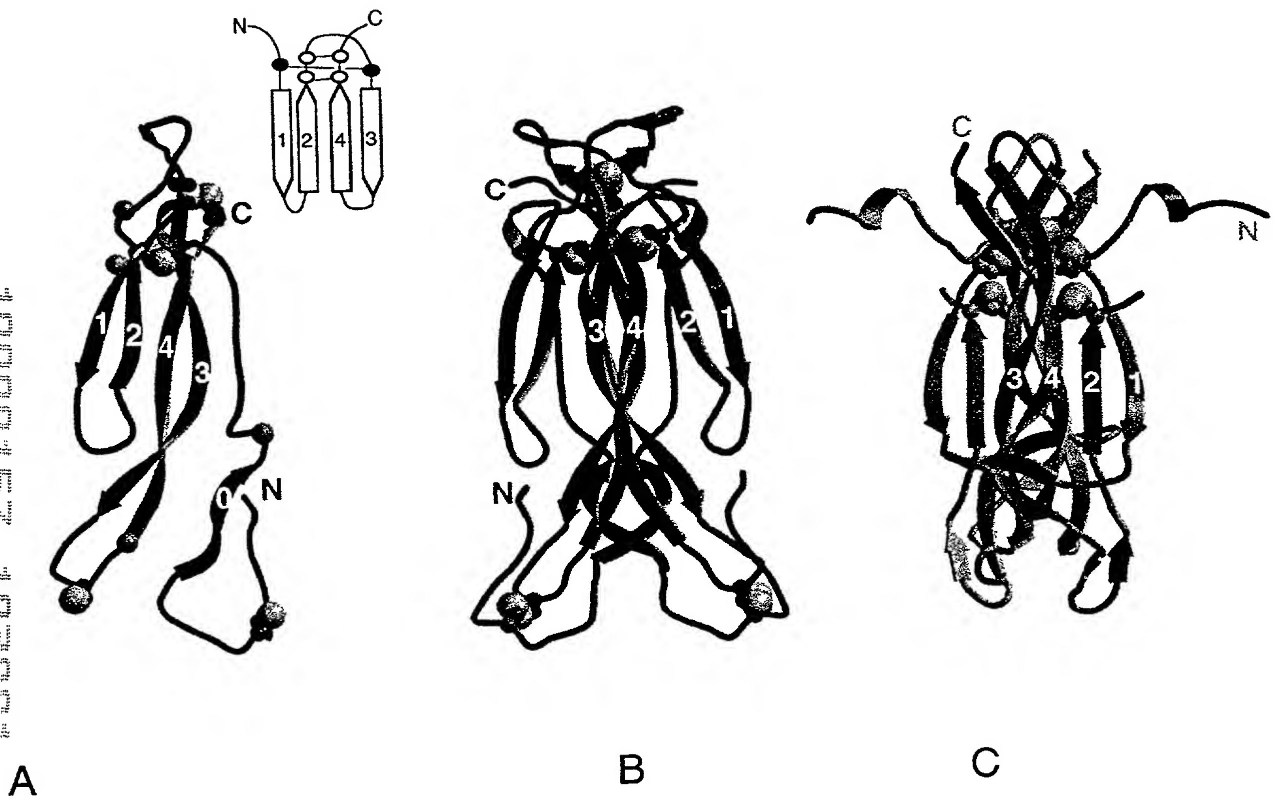


FIGURE 50

```
                                                                        *
IL-17F ..........  ..........  ..........  ...RKIPKVG HTFFQKPESC   17
IL-17A ..........  ..........  ..........  .....IVKAG ITIPRNP.GC   14
IL-17B ......QPRS  PKSKRKGQGR  PGPLAPGPHQ  VPLDLVSRMK PYARMEEYER   44
IL-17C HHDPSLRGHP  HSHGTPHCYS  AEELPLGQAP  PHLLARGAKW GQALPVALVS   50
IL-17E ..........  ..........  ........YS  HWPSCCPSKG QDTSEELLRW   22

                             0                          1
IL-17F PPVPGG....  ....SMKLDI  GIINENQRVS  MSRNIESRST  PWNYTVTWD   59
IL-17A PNSEDKNFPR  TVMVNLNIHN  RNTNTN..PK  RSSDYYNRST  PWNLHRNED   62
IL-17B NIEEMVAQLR  ..NSSELAQR  KCEV....NL  QLWMSNKRSL  PWGYSINHD   88
IL-17C SLEAASHRGR  ..HERPSATT  QCPVLRPEEV  LEADTHQRSI  PWRYRVDTD   98
IL-17E STVPVPPLEP  ..ARPNRHPE  SCRASE....  .DGPLNSRAI  PWRYELDRD   65

                       2                          3
IL-17F PNRYPSEVVQ  AQCRNLGCIN  A..QGKEDIS  MN VPI.QQE TLVVRRKHQG  106
IL-17A PERYPSVIWE  AKCRHLGCIN  A..DGNVDYH  MN VPI.QQE ILVLRREPPH  109
IL-17B PSRIPVDLPE  ARCLCLGCVN  PF.TMQEDRS  MV VPV.FSQ VPVRRR...L  133
IL-17C EDRYPQKLAF  AECLCRGCID  AR.TGRETAA  LN VRL.LQS LLVLRR..RP  144
IL-17E LNRLPQDLYH  ARCLCPHCVS  LQTGSHMDPR  GN ELLYHNQ TVFYRRP...  112

                                   4
        *
IL-17F CSV.......  ....SFQLEK  VL..VTVGCT  CVTPVIHHVQ ...        133
IL-17A CPN.......  ....SFRLEK  IL..VSVGCT  CVTPIVHHVA ...        136
IL-17B CPPPPRTGP.  .....CRQRA  VMETIAVGCT  CIF....... ...        160
IL-17C CSRDGSGLPT  PGAFAFHTEF  IH..VPVGCT  CV.LPRSVAA ALE        184
IL-17E CHGEKGTHKG  .....YCLER  RLYRVSLACV  CVRPRVMG.. ...        145
```

FIGURE 51

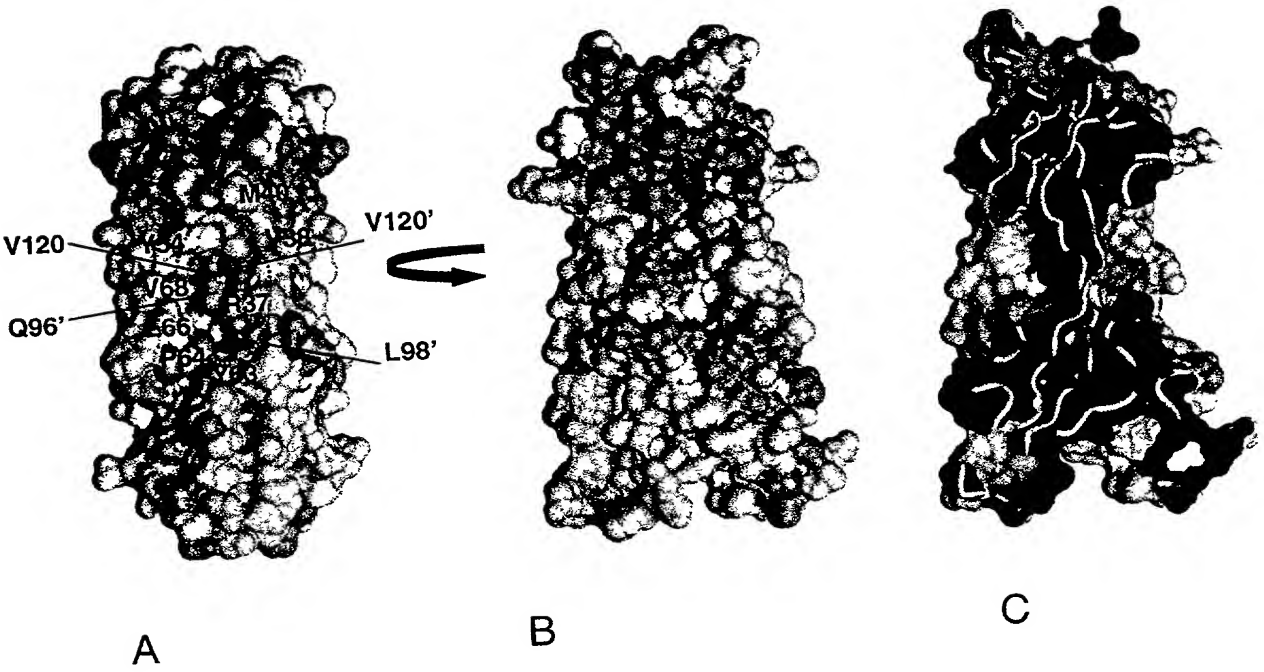


FIGURE 52

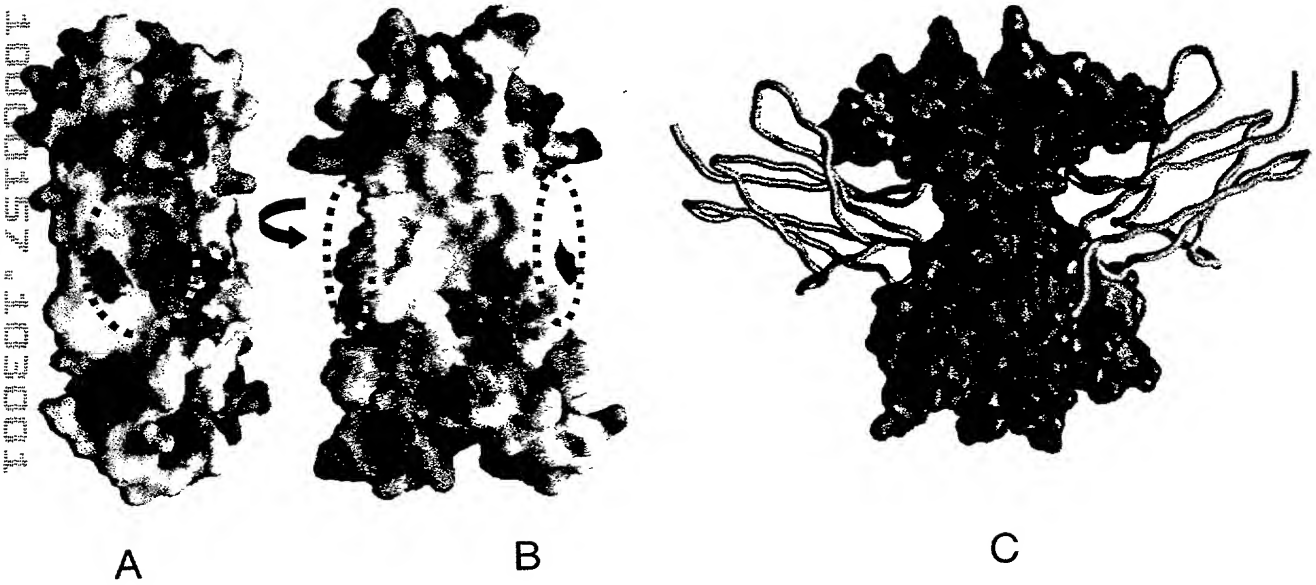
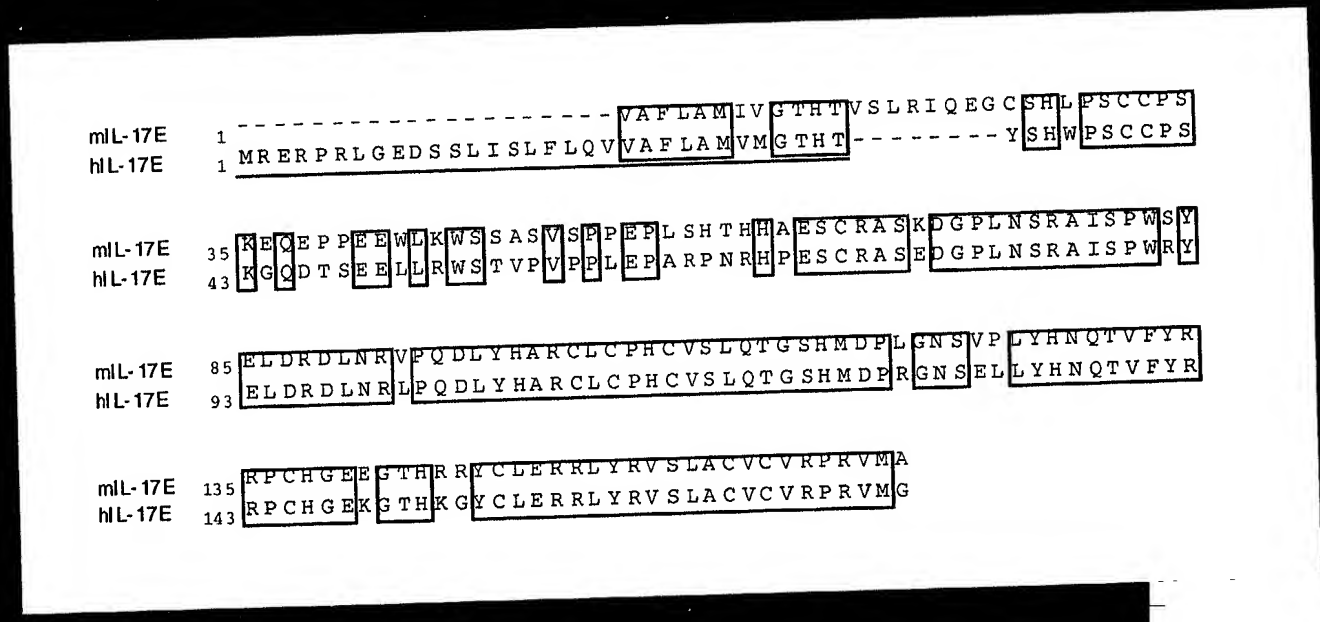


FIGURE 53

IL-17E is highly conserved between human and mouse



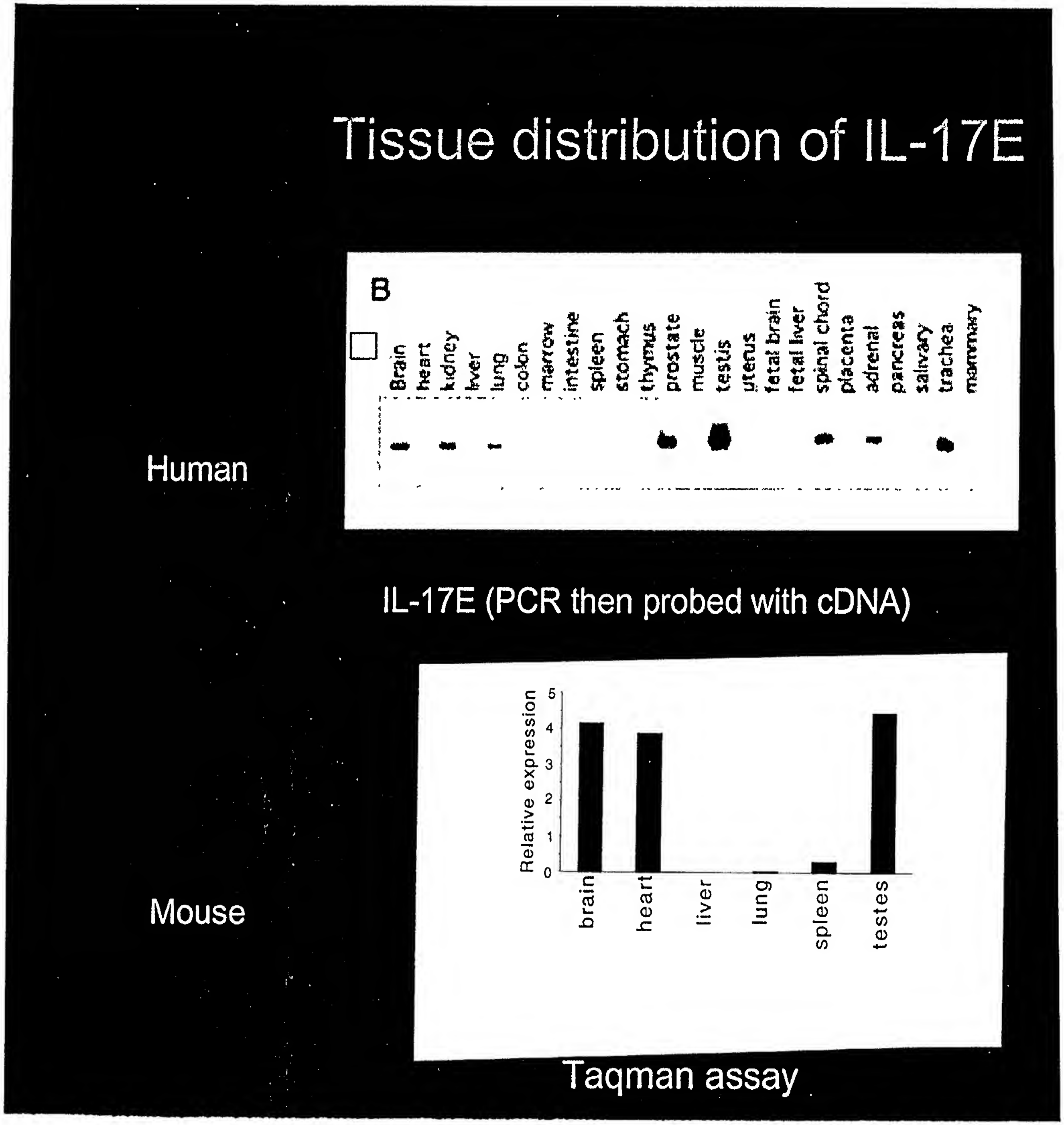

Tissue distribution of IL-17E
Human
B
Brain
heart
kidney
liver
lung
colon
marrow
intestine
spleen
stomach
thymus
prostate
muscle
testis
uterus
fetal brain
fetal liver
spinal chord
placenta
adrenal
pancreas
salivary
trachea
mammary
IL-17E (PCR then probed with cDNA)
Mouse
Relative expression
0
1
2
3
4
5
brain
heart
liver
lung
spleen
testes
Taqman assay

FIGURE 54

FIGURE 55

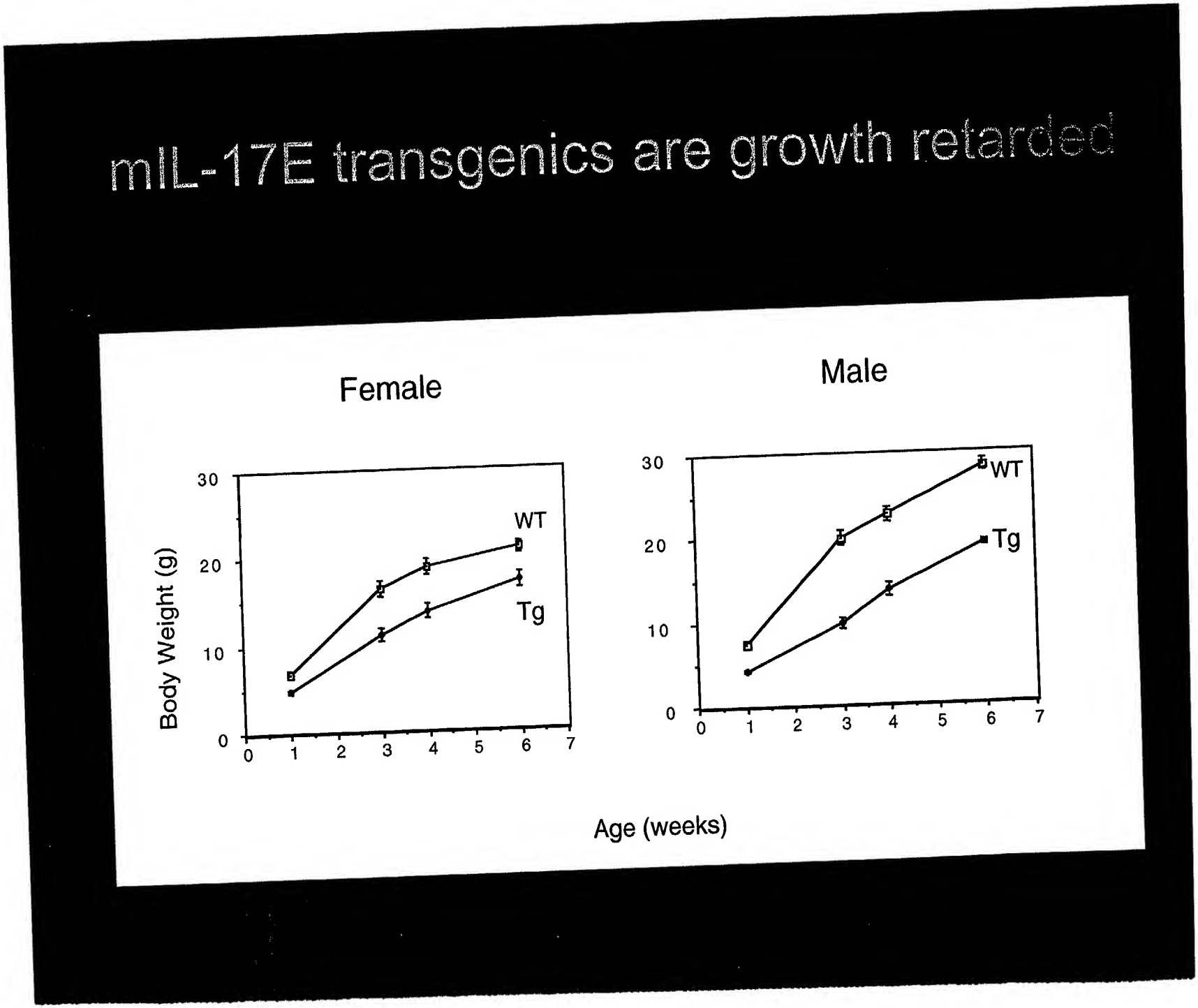

mIL-17E transgenics are growth retarded
Female
Male
Body Weight (g)
WT
Tg
WT
Tg
0
10
20
30
0
1
2
3
4
5
6
7
Age (weeks)

FIGURE 56

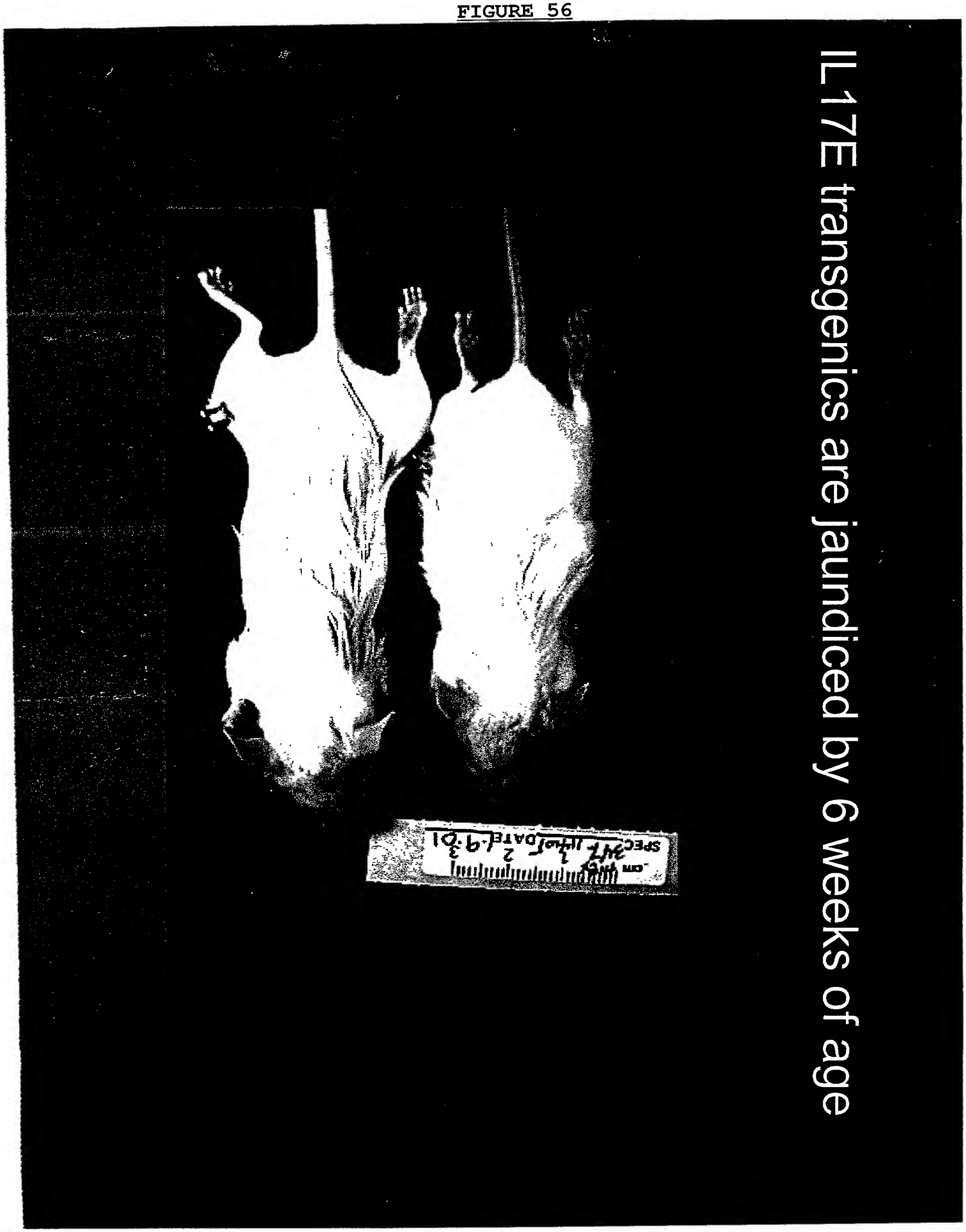
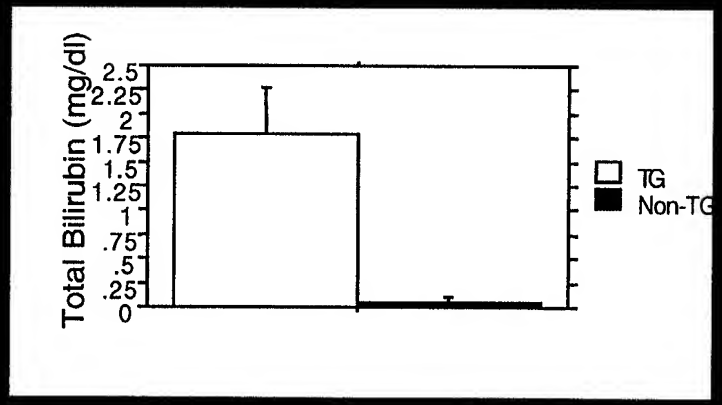
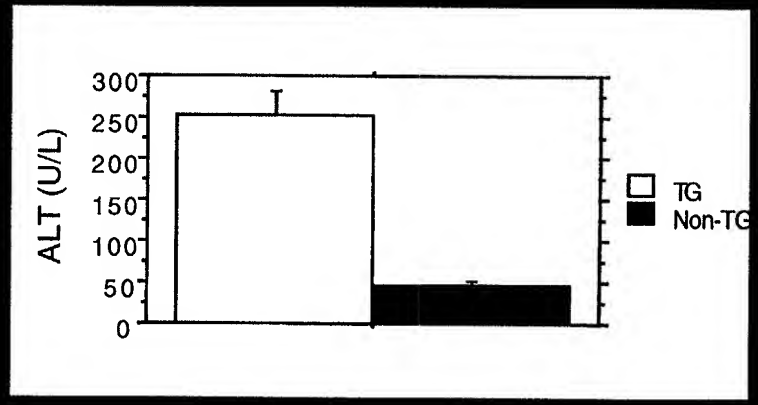
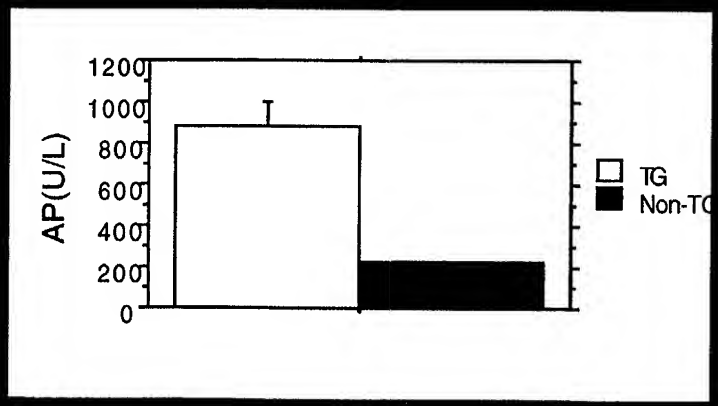


FIGURE 57

mIL-17E transgenics have elevated total bilirubin and liver enzymes







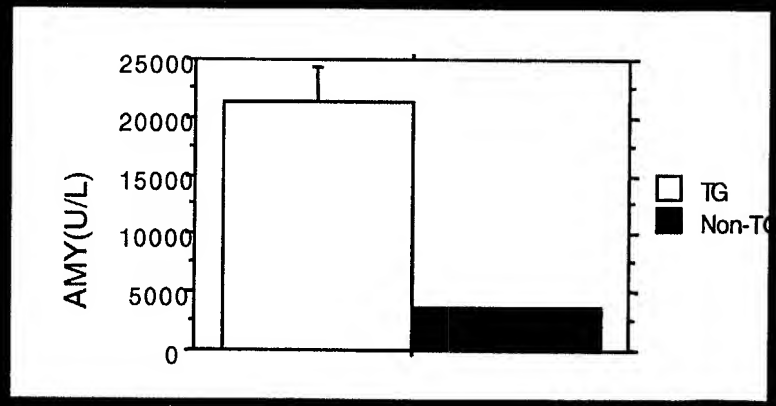
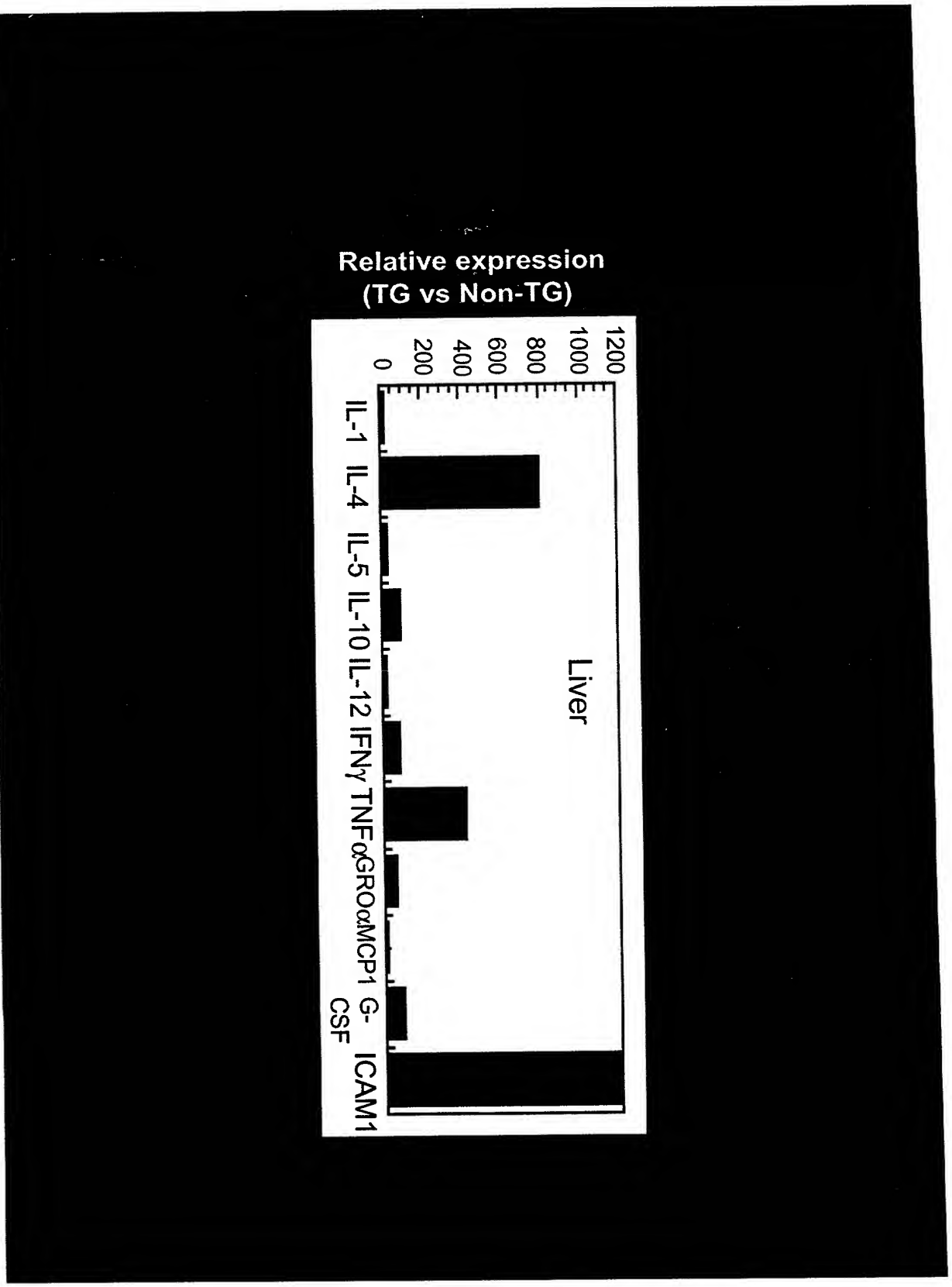
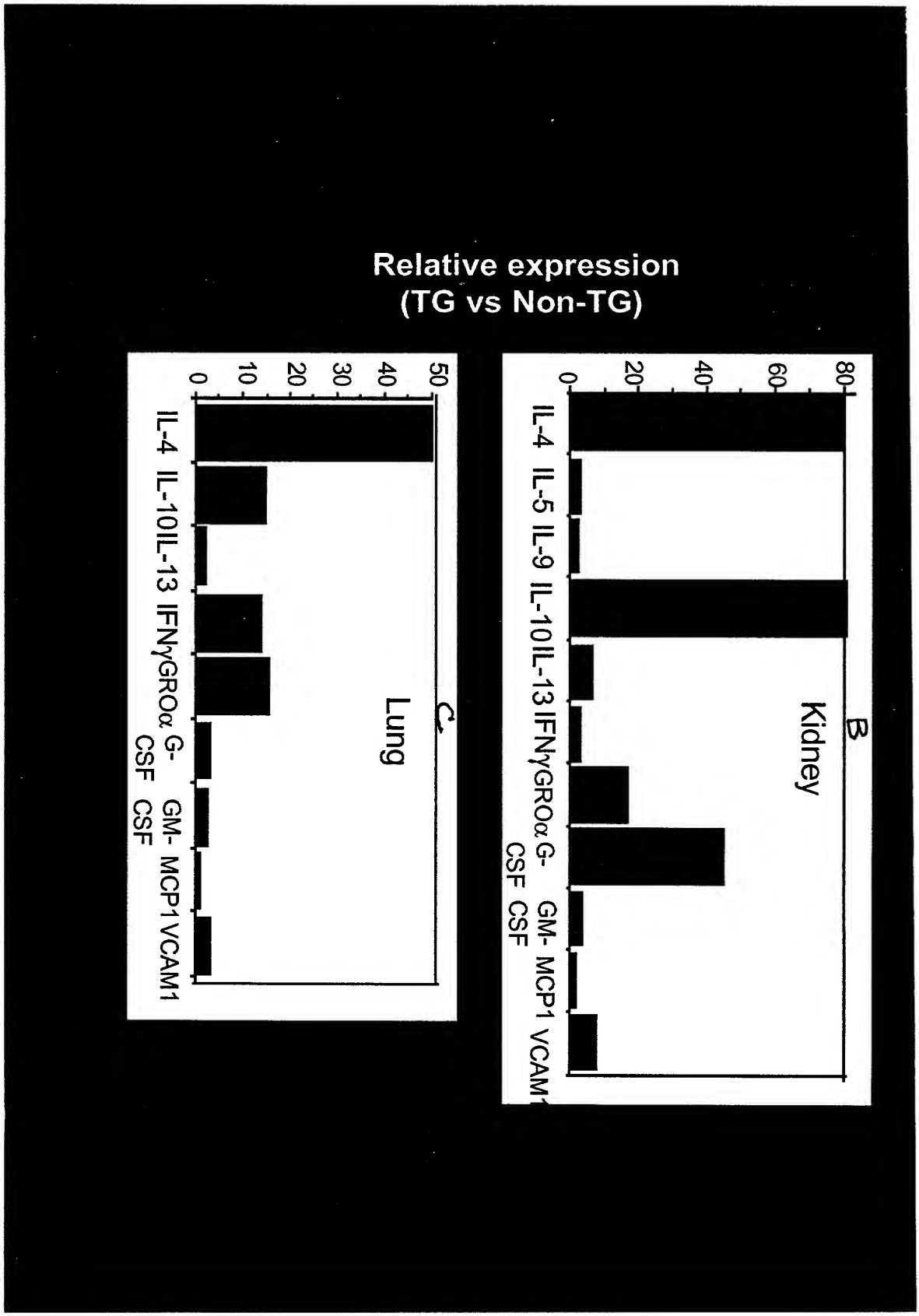
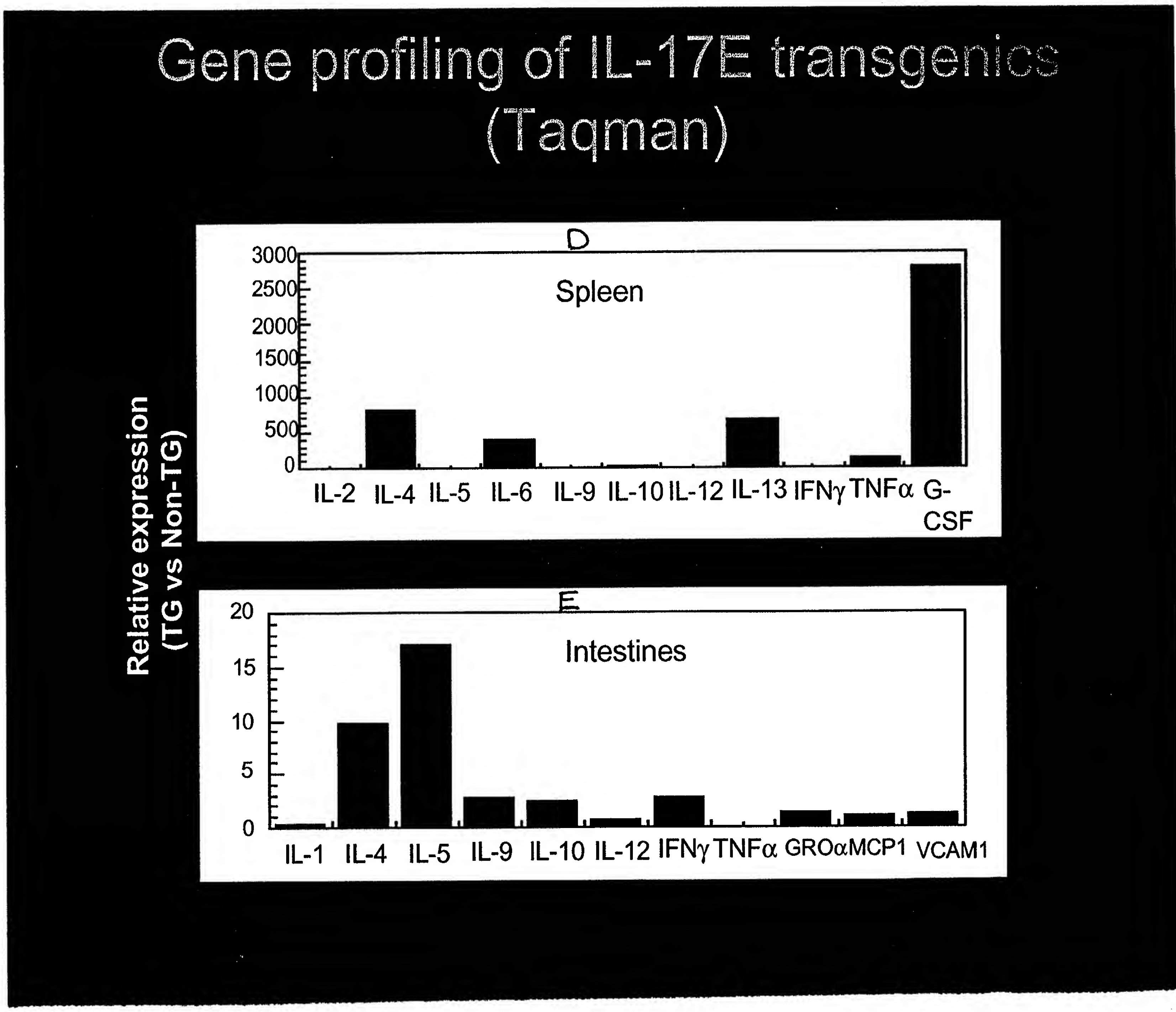


FIGURE 58A


Relative expression
(TG vs Non-TG)
0
200
400
600
800
1000
1200
Liver
IL-1
IL-4
IL-5
IL-10
IL-12
IFNγ
TNFα
GROα
MCP1
G-CSF
ICAM1

FIGURES 58B - 58C





FIGURES 58D - 58E

FIGURE 59

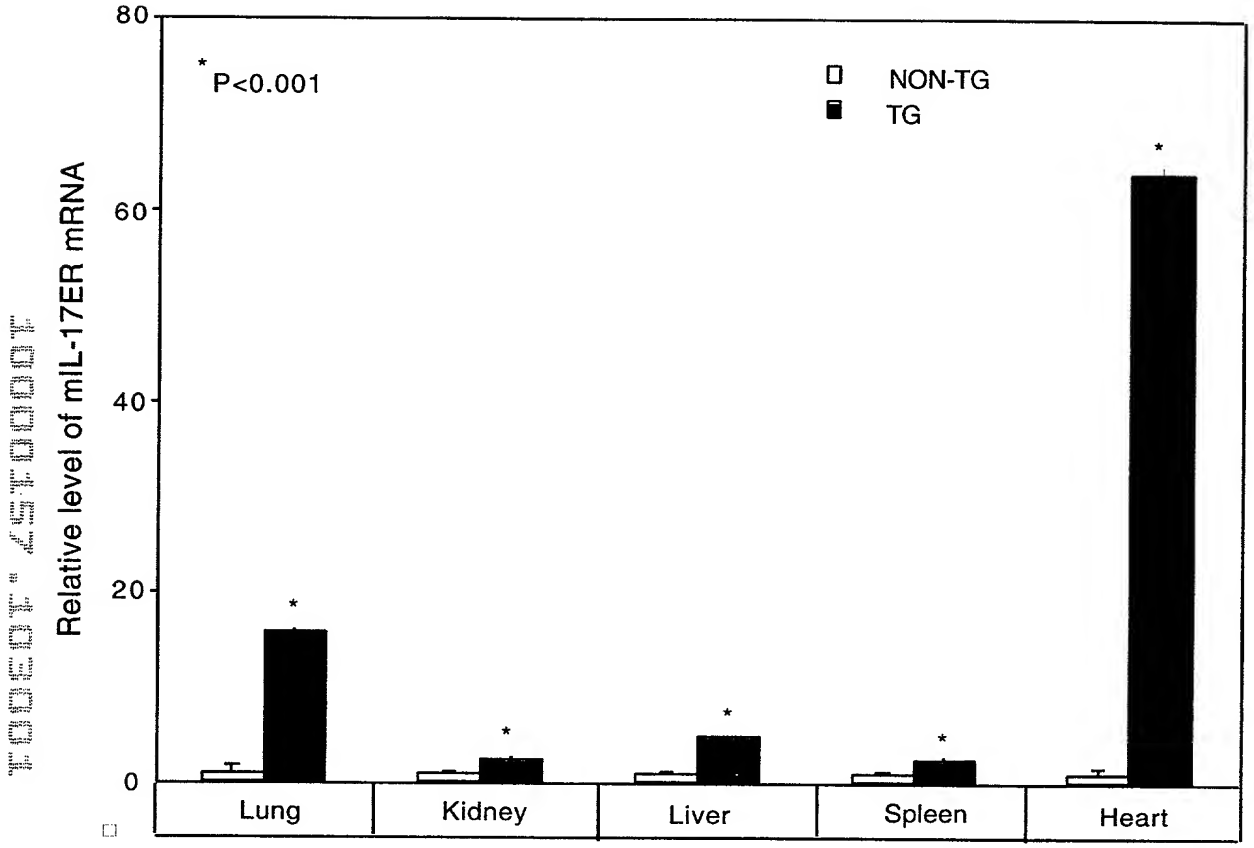

80
60
40
20
0
Relative level of mIL-17ER mRNA
*P<0.001
NON-TG
TG
*
*
*
*
*
Lung
Kidney
Liver
Spleen
Heart

FIGURE 60

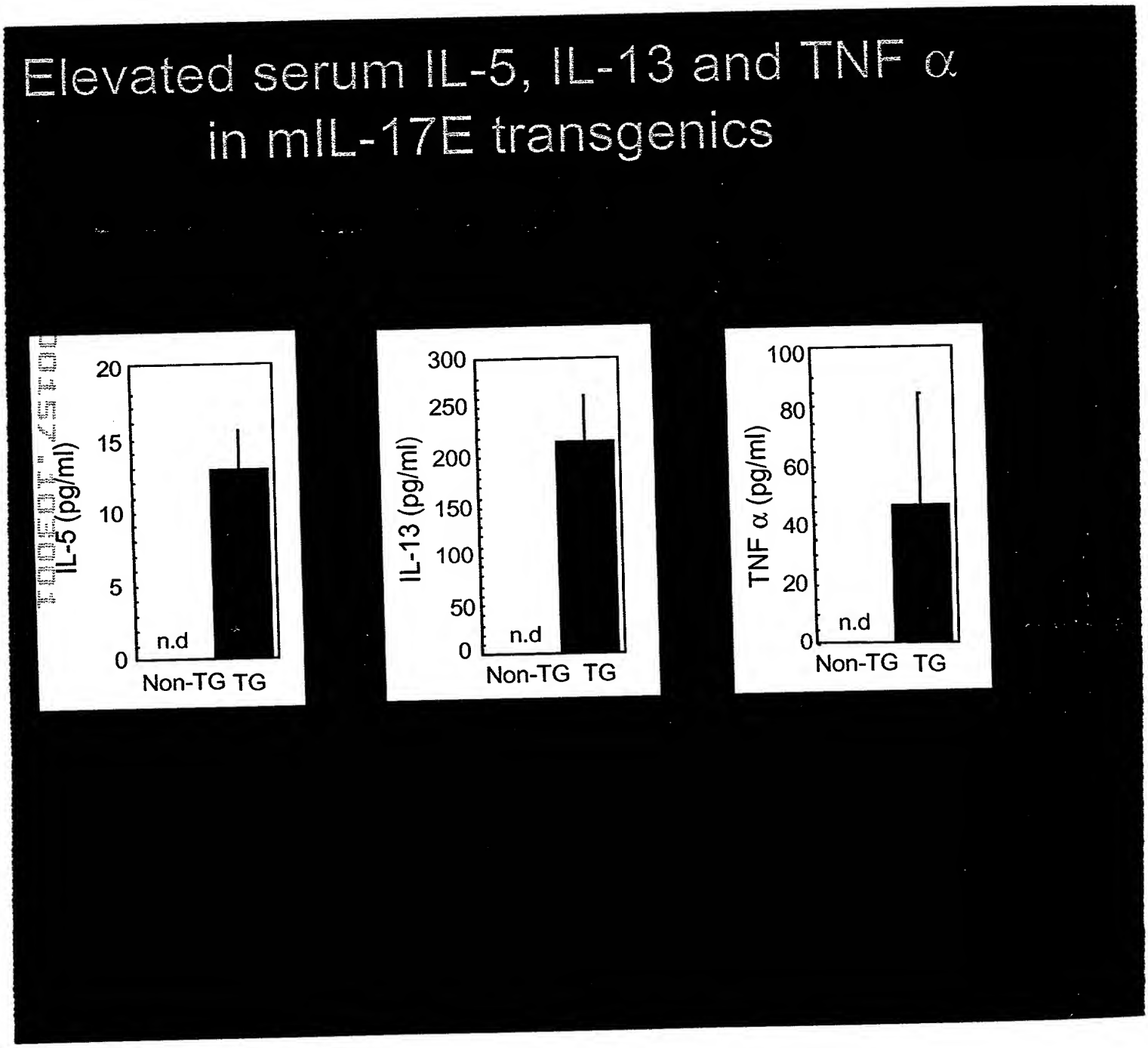

Elevated serum IL-5, IL-13 and TNF α in mIL-17E transgenics
IL-5 (pg/ml)
20
15
10
5
0
n.d
Non-TG TG
IL-13 (pg/ml)
300
250
200
150
100
50
0
n.d
Non-TG TG
TNF α (pg/ml)
100
80
60
40
20
0
n.d
Non-TG TG

FIGURE 61

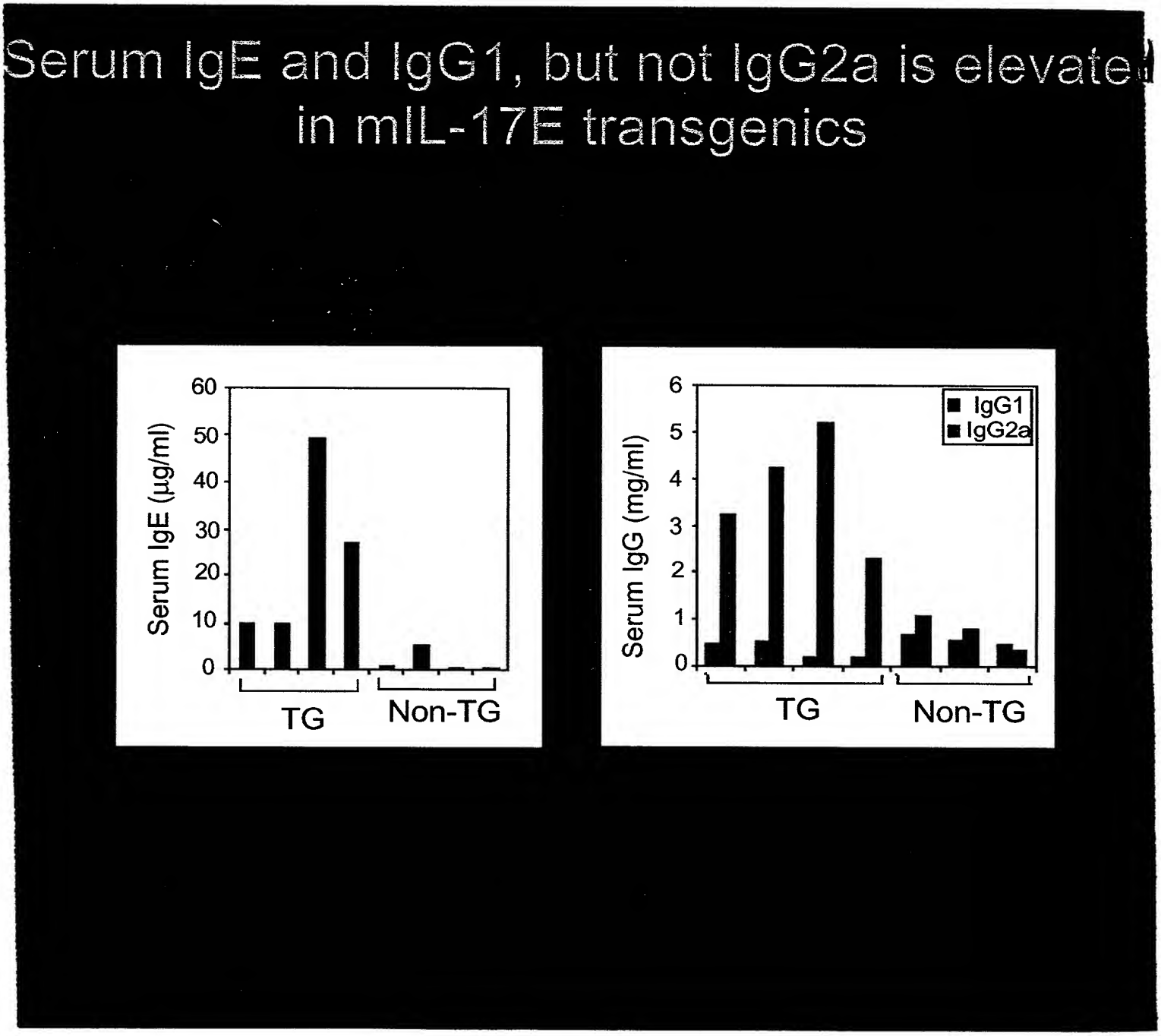

Serum IgE and IgG1, but not IgG2a is elevated in mIL-17E transgenics
Serum IgE (µg/ml)
60
50
40
30
20
10
0
TG
Non-TG
Serum IgG (mg/ml)
6
5
4
3
2
1
0
IgG1
IgG2a
TG
Non-TG

FIGURE 62

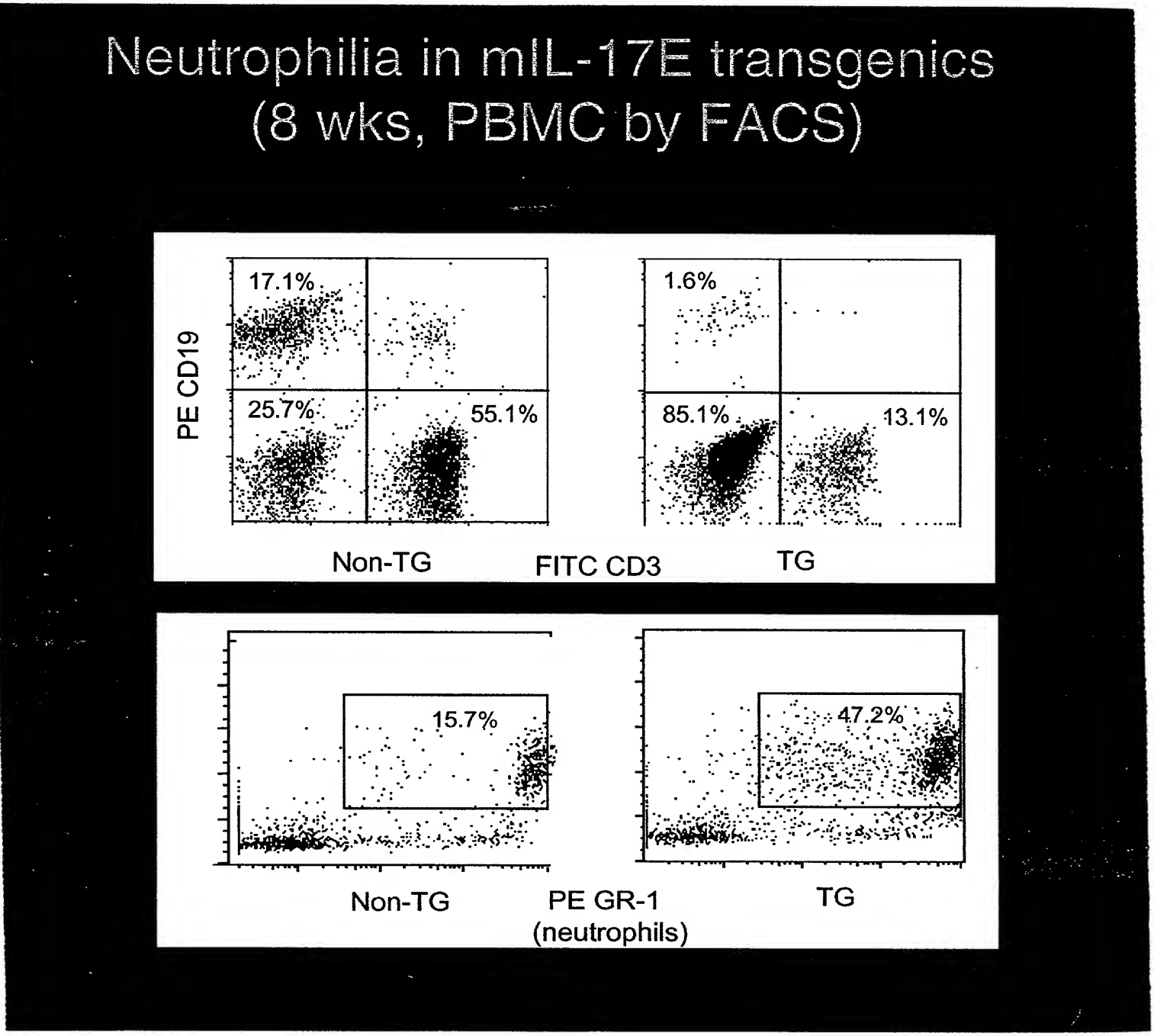

Neutrophilia in mIL-17E transgenics
(8 wks, PBMC by FACS)
PE CD19
17.1%
25.7%
55.1%
1.6%
85.1%
13.1%
Non-TG
FITC CD3
TG
15.7%
47.2%
Non-TG
PE GR-1
(neutrophils)
TG

FIGURE 63

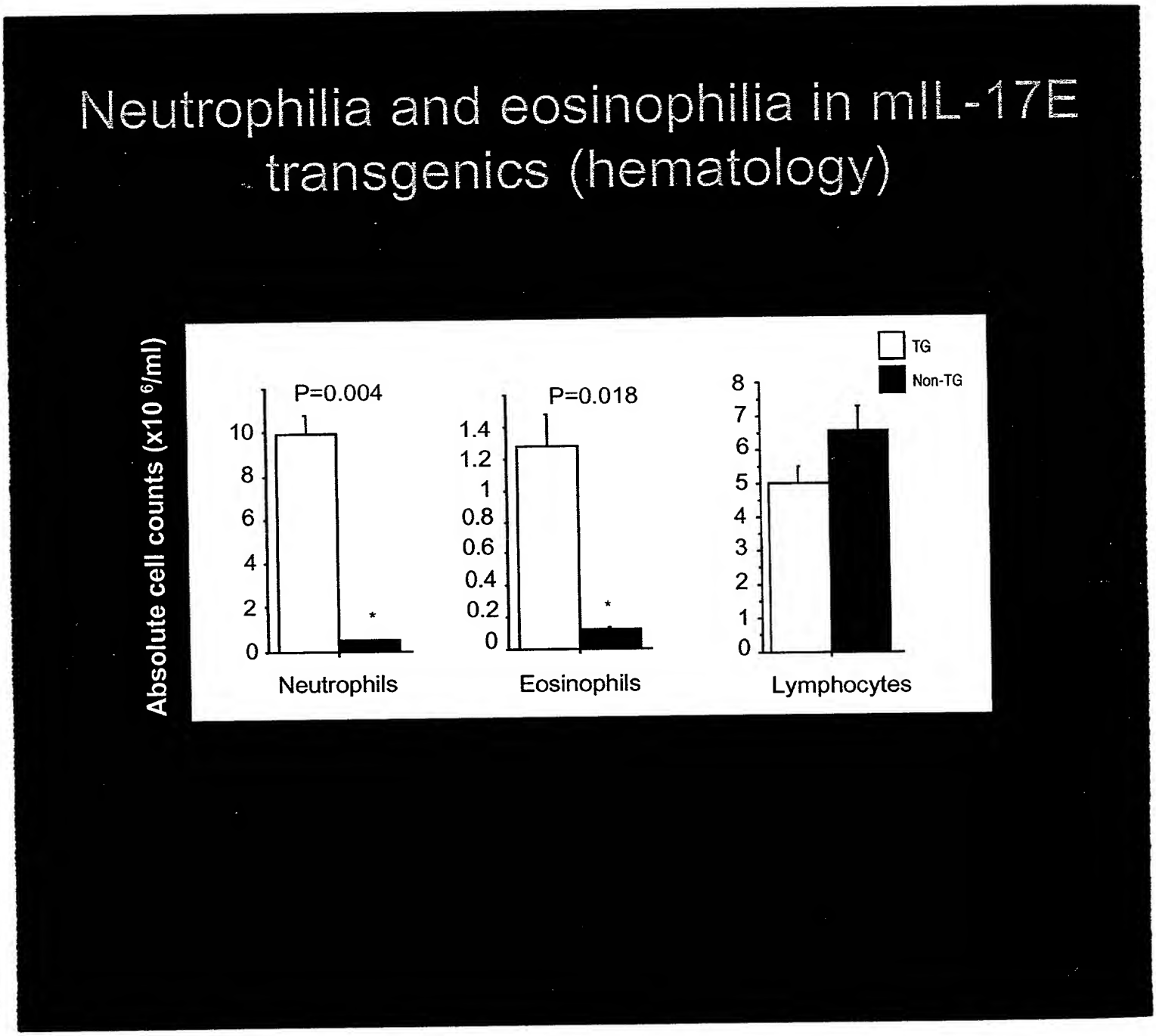

Neutrophilia and eosinophilia in mIL-17E transgenics (hematology)
Absolute cell counts (x10 6/ml)
P=0.004
P=0.018
TG
Non-TG
Neutrophils
Eosinophils
Lymphocytes

FIGURE 64

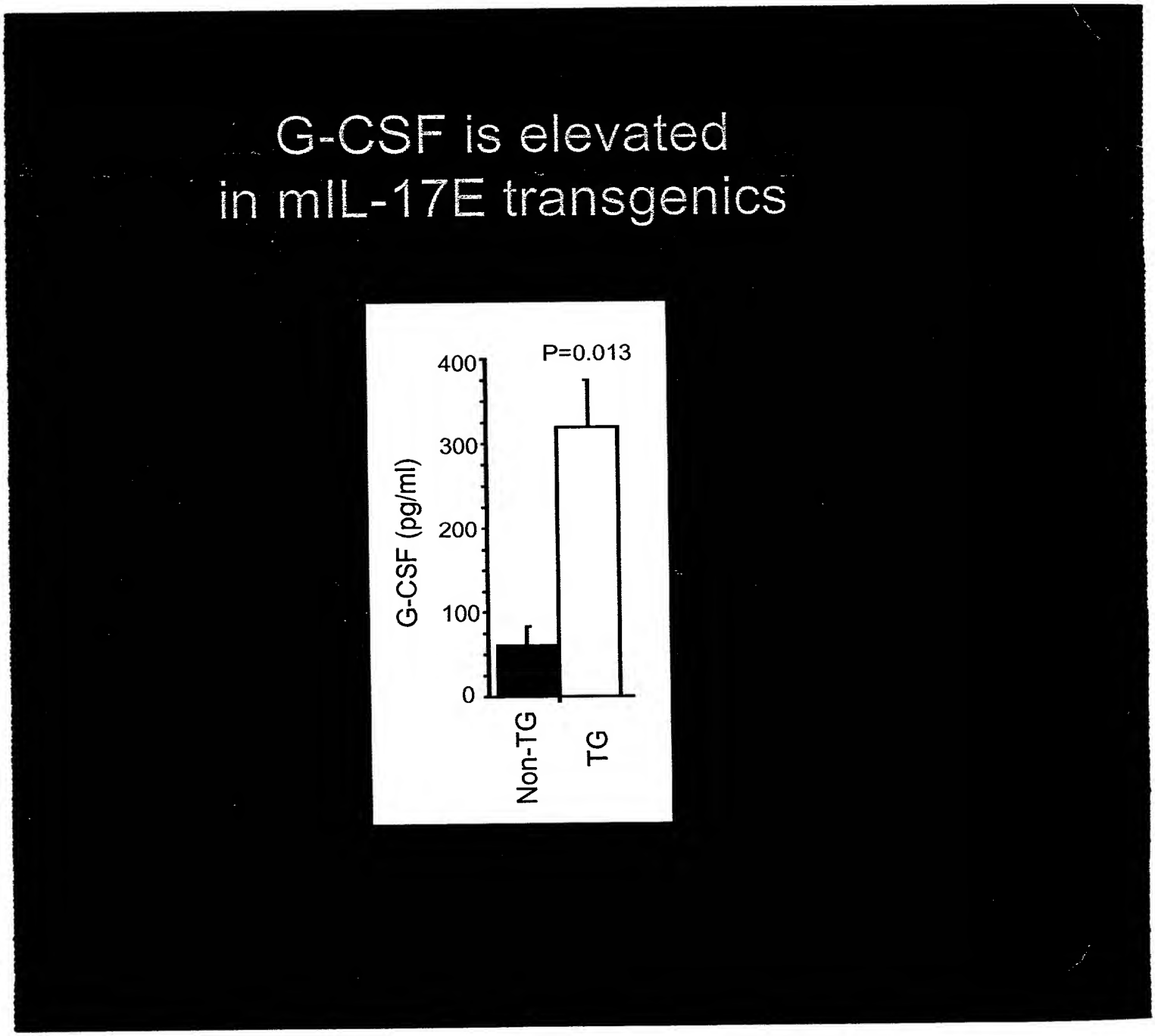

G-CSF is elevated
in mIL-17E transgenics
P=0.013
400
300
200
100
0
G-CSF (pg/ml)
Non-TG
TG

FIGURE 65

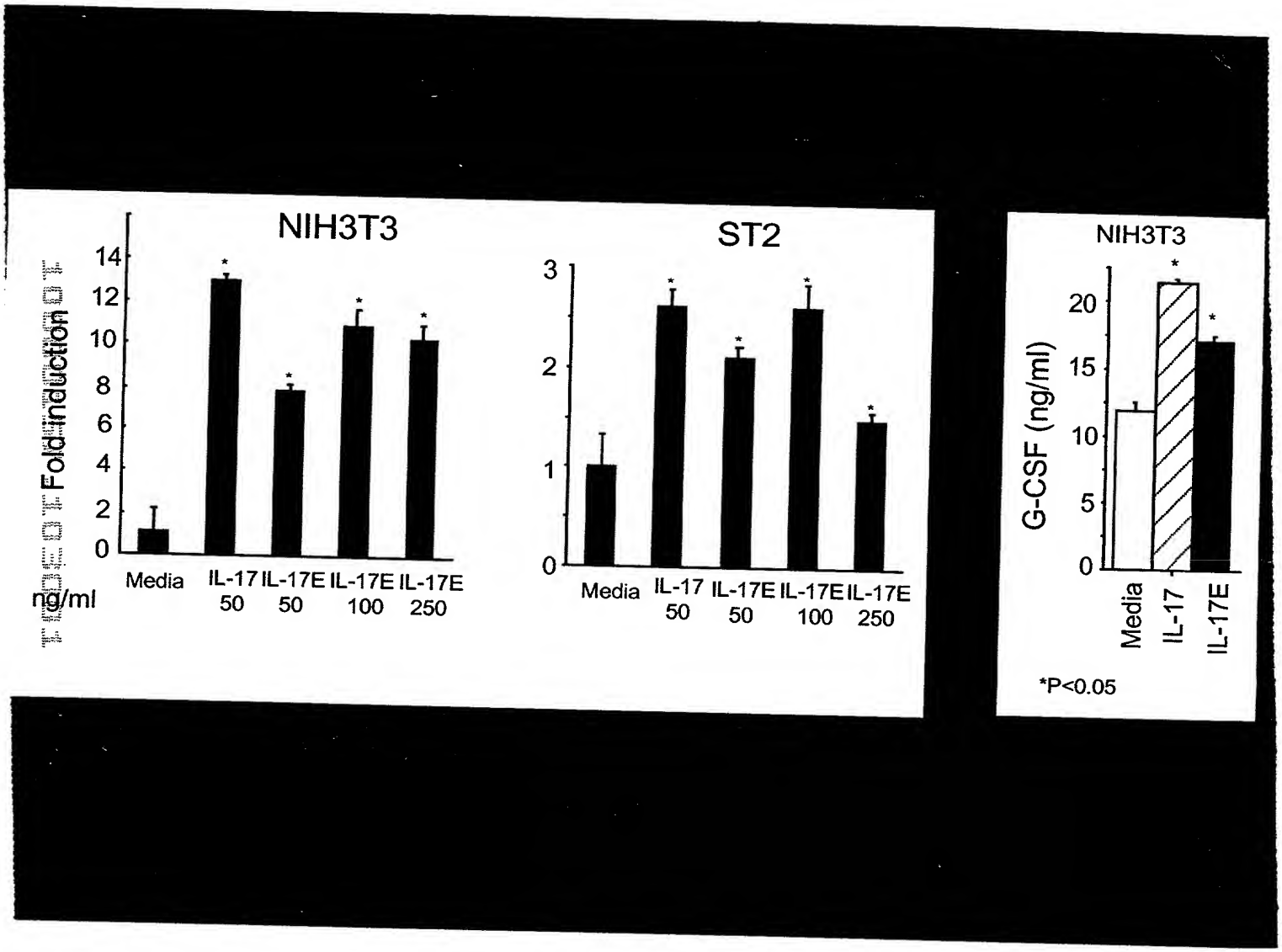

NIH3T3
Fold induction of
14
12
10
8
6
4
2
0
Media
IL-17 50
IL-17E 50
IL-17E 100
IL-17E 250
ng/ml
ST2
3
2
1
0
Media
IL-17 50
IL-17E 50
IL-17E 100
IL-17E 250
NIH3T3
G-CSF (ng/ml)
20
15
10
5
0
Media
IL-17
IL-17E
*P<0.05

FIGURE 66